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XUM

283. *Syntheses in the Colchicine Series. Part III.* The Disposition of the Oxygen Functions in Colchicine.*

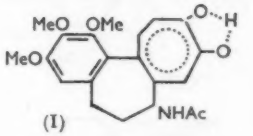
By H. J. E. Loewenthal.

The position of the carbonyl and the methoxyl groups in ring c of colchicine has been proved to be as in (II), by total synthesis of the degradation product (XXIII).

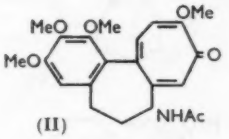
Two brilliant total syntheses of colchicine have recently been announced.[1,2] Formally, both are syntheses of the tautomeric tropolone colchiceine (I), and hence they do not differentiate between colchicine and isocolchicine which are obtained in roughly equal amounts from colchiceine by methylation with diazomethane.[3]

Confirmation of structure (II) for colchicine and hence of (III) for isocolchicine is the subject of the present paper.

An unambiguous synthesis of the *trans*-ketal-acid (IVa) from pyrogallol and glutaric acid was described in previous Parts of this series.[4] Reaction of the toluene-*p*-sulphonate of the derived alcohol (IVb) with di-t-butyl sodiomalonate led to the keto-acid (V), which was cyclised in polyphosphoric acid to the tricyclic diketone (VI). Differentiation between the two ketonic groups in this was accomplished by partial catalytic hydrogenation to the hydroxy-ketone (VII), whose dehydration with acid led in high overall yield to the unsaturated ketone (VIII).



(I)



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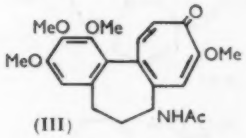

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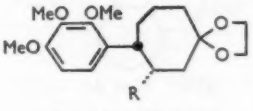
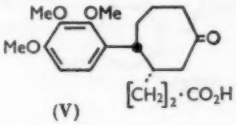
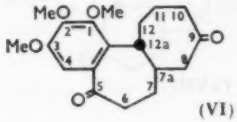


IVa: R = CO_2H

IVb: R = CH_2·OH



(V)



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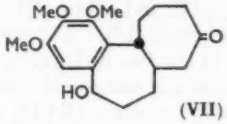
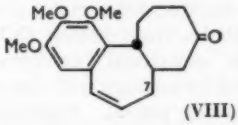


(VII)



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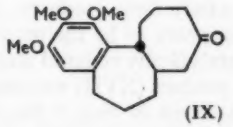

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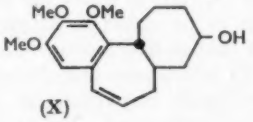
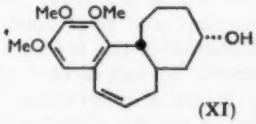


(X)



(XI)

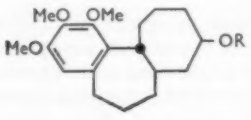
Several attempts were made to oxidise both this ketone (VIII) and its (non-crystalline) ethylene glycol ketal at the allylic 7-position. These included oxidation with selenium

* Part II, *J.*, 1958, 1367.

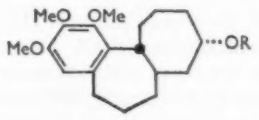
[1] Schreiber, Leimgruber, Pesaro, Schudel, and Eschenmoser, *Angew. Chemie*, 1959, **71**, 637.
[2] Van Tamelen, Spencer, Allen, and Orvis, *J. Amer. Chem. Soc.*, 1959, **81**, 5341.
[3] Sorkin, *Helv. Chim. Acta*, 1946, **29**, 246.
[4] *J.*, 1953, 3962; 1958, 1367.

dioxide in a variety of solvents and with t-butyl chromate, allylic bromination with *N*-bromosuccinimide and reaction of the resulting crude product with sodionitropropane [5] or with dimethyl sulphoxide.[6] They were all unsuccessful and are not described in detail.

Modification of the ketone group in (VIII) to an acyloxy-group was then considered. Reduction with lithium hydridotri-t-butoxyaluminate in tetrahydrofuran [7] was fortunately surprisingly stereoselective, giving a mixture of the non-crystalline unsaturated alcohols (X) and (XI), which, for separation and subsequent reaction, were converted into the acetates or *p*-bromobenzoates. In either case (particularly with the *p*-bromobenzoates) chromatography effected nearly sharp separation of the epimers of which one (series X) was eluted preferentially and was present in the ratio 4 : 1 to the other epimer. The probable configuration and general stereochemistry of these and following compounds will be discussed in the following paper. Similar reduction of the saturated ketone (IX) was even more stereoselective, giving the epimers (XII) and (XIII) in the ratio 5·5 : 1.



(XII)



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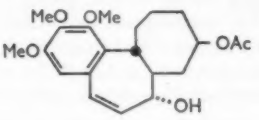
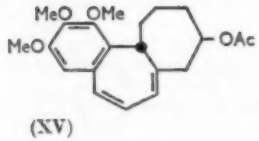
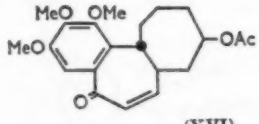


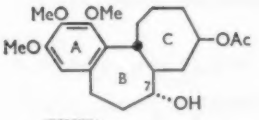
(XIV)



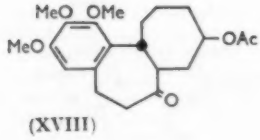
(XV)



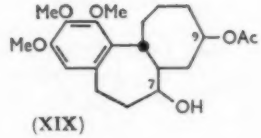
(XVI)



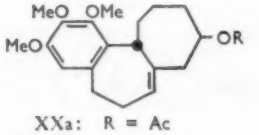
(XVII)



(XVIII)



(XIX)



XXa: R = Ac
XXb: R = H

Oxidation of the unsaturated acetoxy-compound (Xb) with selenium dioxide in pyridine gave mainly three products: the unsaturated acetoxy-alcohol (XIV) and -diene (XV) and what appears to be the unsaturated acetoxy-ketone (XVI) (cf. Part II [4]). The alcohol was catalytically reduced and the " equatorial " conformation of the free hydroxyl group in the product (XVII) was assumed by analogy with the corresponding compound without a substituent in ring C (see following paper). Oxidation of this product (XVII) with chromic oxide in pyridine gave the saturated acetoxy-ketone (XVIII) in which the *trans*-junction between the two seven-membered rings appeared to be stable in attempted epimerisation at position 7a. Reduction of this ketone with lithium hydridotri-t-butoxyaluminate gave in turn the epimeric acetoxy-alcohol (XIX) which was dehydrated to the acetoxy-monoene (XXa) by means of phosphorus oxychloride in pyridine or (preferably) by the action of collidine on the 9-acetate-7-methanesulphonate.[8] The product from the former reaction was contaminated by the derived 7-chloride.

Treatment with hydrogen chloride in chloroform failed to rearrange the double bond

[5] Montavan, Lindlar, Marbet, Ruegg, Ryser, Saucy, Zeller, and Isler, *Helv. Chim. Acta*, 1957, **40**, 1250.

[6] Kornblum, Powers, Anderson, Jones, Larson, Levand, and Weaver, *J. Amer. Chem. Soc.*, 1957, **79**, 6562.

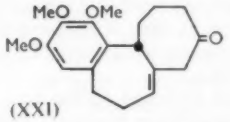
[7] Brown and McFarlin, *J. Amer. Chem. Soc.*, 1958, **80**, 5372.

[8] Cf. Heusler and Wettstein, *Helv. Chim. Acta*, 1952, **35**, 284.

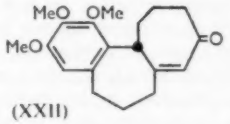
of the unsaturated acetate (XXa) to a position conjugated to the aromatic ring, and the compound was recovered unchanged. This was surprising in view of the successful prototropic rearrangement of the ring-C unsubstituted analogue.[9] Possibly the acetoxy-group prevents access of a proton to the double bond, as does the spirostan or 20-oxopregnane side chain in certain $\Delta^{8,14}$-steroids.[10]

On the other hand, the $\beta\gamma$-unsaturated ketone (XXI), obtained by oxidation of the alcohol (XXb) with chromic oxide in pyridine, isomerised smoothly to the non-crystalline ketone (XXIII) on treatment with toluene-*p*-sulphonic acid in acetone. By following this isomerisation in chloroform containing hydrogen chloride in the infrared spectrograph it was clear that it did not proceed *via* the $\alpha\beta$-unsaturated ketone (XXII). The ketone (XXIII) gave a crystalline ethylene ketal which was kindly compared by Professor Rapoport (University of California) with the corresponding product of degradation of colchicine [11] and found to be identical with it.

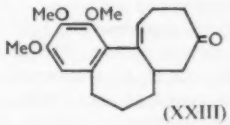
The unambiguity of the degradation of colchicine (II) to this ketal *via* *NN*-dimethylaminocolchicide (XXIV) and the keto-amide (XXV) has been discussed in detail by Rapoport and his co-workers.[11,12] As they point out, the ketone group in colchicine (II) and in the ketone (XXV) is undoubtedly at the same position in ring C, since both compounds on hydrogenation give the same hydroxy-amide (XXVI); and the conversion [11] of the amide (XXV) into the ethylene ketal of ketone (XXIII) cannot introduce a further element of uncertainty on this point. The only problem remaining is that of the position of the non-reducible styrene double bond in compounds (XXIII) and (XXV). The



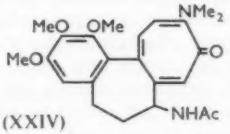
(XXI)



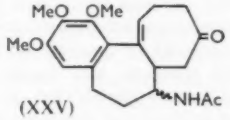
(XXII)



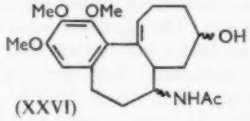
(XXIII)



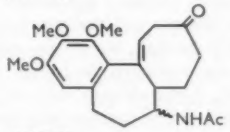
(XXIV)



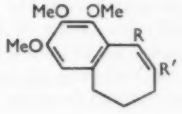
(XXV)



(XXVI)



(XXVII)



XXVIIIa: R = R' = H
XXVIIIb: R = Me, R' = H
XXVIIIc: R = R' = Me

ultraviolet spectra of these two compounds are very similar.[11] Muller and Velluz [13] have shown that the cyano-diene obtained from (XXV) by conversion into the cyanohydrin and subsequent dehydration has ultraviolet absorption similar to that of (XXV) ($\lambda_{max.}$ 251 mμ), while the corresponding compound obtained from the keto-amide derived from isocolchicine (XXVII) showed evidence of extended conjugation ($\lambda_{max.}$ 268 mμ). On the assumption that the styrene double bond in (XXV) and (XXVII) is tetra-substituted they concluded that the carbonyl groups in colchicine and isocolchicine should be placed at positions 10 and 9 respectively. Against this, Forbes [14] suggested placing the double

[9] Loewenthal and Rona, *Proc. Chem. Soc.*, 1958, 114, and the following paper.
[10] Mancera, Barton, Rosenkranz, and Djerassi, *J.*, 1952, 1021.
[11] Rapoport, Campion, and Gordon, *J. Amer. Chem. Soc.*, 1955, **77**, 2389.
[12] Rapoport, Williams, Campion, and Pack, *J. Amer. Chem. Soc.*, 1954, **76**, 3693.
[13] Muller and Velluz, *Bull. Soc. chim., France*, 1955, 1452.
[14] Forbes, *Chem. and Ind.*, 1956, 192.

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bond at the trisubstituted 12,12a-position,[15] and this would correlate the position now established for the carbonyl group in the ketone (XXIII) with Muller and Velluz's results and with our conclusions (see following paper) that owing to the strained nature of the cycloheptadiene ring one of the double bonds in such a system would tend to move to an exocyclic position if this is structurally and energetically possible.

Gardner and his co-workers [16] have commented that the ultraviolet absorption of the ketal (as XXIII) and the amide (XXV) ($\lambda_{max.}$ 256 ± 3 mμ) violates Woodward's rules regarding the effect of substitution on a conjugated double bond, when compared with that of the trimethoxybenzocyclohepta-1,3-diene (XXVIIIa) ($\lambda_{max.}$ 264 mμ). The methyl-substituted homologues (XXVIIIb and c) were prepared; and examination of their ultraviolet spectra shows that here, too, substitution at the double bond leads to a hypsochromic shift. Clearly this is due to steric interference by the neighbouring aromatic methoxyl group.

Experimental

Infrared spectra refer to $CHCl_3$ solutions, and ultraviolet spectra to MeOH (Spectrograde) solutions.

β-trans-2-(2,3,4-*Trimethoxyphenyl*-6-*oxo*)*cycloheptylpropionic Acid* (V).—*trans*-6,6-Ethylenedioxy-2-(2,3,4-trimethoxyphenyl)cycloheptanecarboxylic acid (IVa) (20 g.), dissolved in dry tetrahydrofuran (50 ml.), was added dropwise with stirring to a solution of lithium aluminium hydride (5·5 g.) in boiling ether (150 ml.). Heating under reflux was continued for another 4 hr. and the mixture then decomposed with Rochelle salt solution. After addition of benzene the organic layer was washed with 10% sodium hydroxide solution and water, dried ($MgSO_4$), and evaporated *in vacuo*. The remaining crude trans-6,6-*ethylenedioxy*-2-(2,3,4-*trimethoxyphenyl*)*cycloheptylmethanol* (IVb) (18·0 g.) was used directly for the next step; a sample distilled evaporatively at 200—210° (bath)/10^{-2} mm. as a colourless very viscous oil (Found: C, 64·45; H, 8·05. $C_{19}H_{28}O_6$ requires C, 64·75; H, 8·0%), $\nu_{max.}$ 2·82 and 6·24 μ.

This crude alcohol (18·0 g.) was dissolved in dry pyridine (55 ml.) and cooled to −10°. Toluene-*p*-sulphonyl chloride (12·4 g.) was added and the resulting solution kept at −5° overnight, after which it was decomposed by cautious addition of 10% potassium hydrogen carbonate solution. The oil which separated was extracted with ether–benzene; the extract was washed several times with water, then with ice-cold 10% acetic acid (300 ml.), again with water, with 10% potassium hydrogen carbonate solution, and finally with saturated sodium chloride solution. The dried ($MgSO_4$) extract was concentrated *in vacuo* below 40°. The remaining oil (no OH band; bands at 7·35 and 8·53 μ) was dissolved in toluene (30 ml.) and added to a suspension of di-t-butyl sodiomalonate, prepared from the ester (23 g.) and sodium hydride (2·1 g.) in benzene (30 ml.) and toluene (30 ml.). After 30 hours' refluxing, water was added; the organic layer was separated and dried and the solvents were removed *in vacuo*. The residue was heated under reflux with acetic acid (200 ml.) and 4% hydrochloric acid (80 ml.) for 15 hr., after which the solvents were removed *in vacuo* at 100°. The residue was heated for 15 min. at 200°, cooled, and taken up in ether–benzene. The organic layer was extracted several times with 5% potassium carbonate solution; acidification of the extracts gave the crude *keto-acid* (13·9 g.) which was isolated with ether. Trituration with ether–cyclohexane (2 : 1) gave needles (8·8 g.), m. p. 110—112°; further crystallisation from ether raised the m. p. to 114·5—115·5° (Found: C, 65·05; H, 7·4. $C_{19}H_{26}O_6$ requires C, 65·1; H, 7·5%); it had infrared band with inflections at 5·80 and 5·85 μ.

5,6,7,7aα,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene*-5,9-*dione* (VI).—The above keto-acid (16·0 g.) was melted by heating to 120°; the melt was cooled and polyphosphoric acid, prepared from 85% orthophosphoric acid (140 ml.) and phosphoric oxide (260 g.), was added. The red solution was heated with stirring at 75—80° for 1 hr., after which it was added to ice. The gum which separated was extracted with ether–benzene, and the organic extract washed with water, 5% sodium hydroxide solution, again with water, dried ($MgSO_4$), and concentrated. The residue was passed in benzene through a short column of activated alumina, the solvent was removed from the eluate, and the residue crystallised from cyclohexane to

[15] Vaterlaus and Muller (*Bull. Soc. chim. France*, 1957, 1329) later came to the same conclusion on more indirect evidence.

[16] Gardner, Brandon, and Haynes, *J. Amer. Chem. Soc.*, 1957, **79**, 6334.

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give the *diketone* (8·1 g.) which after recrystallisation from the same solvent was obtained as needles, m. p. 110—110·5° (Found: C, 68·3; H, 7·4; MeO, 27·5. $C_{19}H_{24}O_5$ requires C, 68·65; H, 7·3; 3MeO, 28%), $\nu_{max.}$ 5·90—5·95 (broad) and 6·26 μ. Chromatography of the mother-liquors gave another 1·0 g. of the diketone.

7,7aα,8,9,10,11,12,12aβ-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-9-*one* (VIII).—The above diketone (1·62 g.) was catalytically reduced in methanol, with a prehydrogenated mixture of 10% palladium–carbon (110 mg.) and 4% palladium–strontium carbonate (110 mg.). Hydrogen absorption was slow and practically ceased after uptake of one mol. The residue of the keto-alcohol (VII), obtained after filtration and removal of solvent (bands at 2·77 and 5·91s μ), was heated for 2 hr. in benzene (50 ml.) with naphthalene-2-sulphonic acid (100 mg.) with azeotropic removal of water. The cooled solution was washed with 5% sodium hydroxide solution and water, then dried ($MgSO_4$), and the solvent was removed. The residue, which crystallised, was purified by chromatography and crystallisation from hexane to give the unsaturated *ketone* (1·46 g.), m. p. 82—83°. Further recrystallisation gave needles, m. p. 87·5—88° (Found: C, 72·3; H, 7·7. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·65%), $\lambda_{max.}$ 259 mμ (ε 11,000), $\lambda_{min.}$ 243 mμ (ε 7400), $\nu_{max.}$ 5·90, 6·26, and 6·40 μ. The *semicarbazone* formed needles (from dilute ethanol), m. p. 187·5—188° (Found: C, 64·5; H, 7·2; N, 11·45. $C_{20}H_{27}N_3O_4$ requires C, 64·3; H, 7·3; N, 11·25%).

Catalytic hydrogenation of the above unsaturated ketone in methanol in the presence of 4% palladium–strontium carbonate was rapid, giving 5,6,7,7aα,8,9,10,11,12,12aβ-*decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-9-*one* (IX), which formed needles, m. p. 118·5—119·0°, from methanol (Found: C, 72·0; H, 8·25. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%), bands at 5·90 μ and 6·25 μ. The 2,4-*dinitrophenylhydrazone*, orange needles from chloroform–ethanol, had m. p. 207—207·5° (Found: C, 59·9; H, 6·05; N, 11·25. $C_{25}H_{30}N_4O_7$ requires C, 60·25; H, 6·05; N, 11·25%).

Esters of 7,7aα,8,9,10,11,12,12aβ-*octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-9-*ols* [β(X)- and α(XI)-*Epimers*).—The unsaturated ketone (VIII) (3·50 g.) was added at 0° to a solution of lithium hydridotri-t-butoxyaluminate (10 g.) in tetrahydrofuran (150 ml.). After being stirred overnight at room temperature the mixture was decomposed by ice-cold 5% hydrochloric acid and the tetrahydrofuran removed *in vacuo*. The crude mixture of epimeric unsaturated alcohols, isolated with ether–benzene, could not be separated into crystalline fractions even after chromatography. It (4·0 g.) was therefore heated with acetic anhydride (7·0 ml.) in pyridine (15·0 ml.) at 100° for 2 hr. The crude mixture of acetates obtained after the usual working-up was chromatographed on activated alumina (Alcoa; 10 g.), with hexane as solvent and methylene chloride–hexane as eluant, giving first the 9β-*acetate* (as X), needles (from hexane), m. p. 98—99° (Found: C, 70·1; H, 7·7. $C_{21}H_{28}O_5$ requires C, 69·95; H, 7·85%), $\nu_{max.}$ 5·81, 6·26, and 6·40 μ, followed by the 9α-*epimer* (as XI), prisms (from hexane), m. p. 78·5—79·5° (Found: C, 70·2; H, 7·75%), $\nu_{max.}$ 5·81, 6·25, and 6·40 μ.

Alternatively, and for a sharper chromatographic separation, the crude alcohol mixture (3·30 g.) was heated at 50—60° for 1 hr. with *p*-bromobenzoyl chloride (2·50 g.) in pyridine (17·0 ml.). The crude product obtained after the usual working-up was likewise chromatographed in hexane on alumina (Alcoa; 100 g.), giving first the 9β-p-*bromobenzoate* (as X), which after several recrystallisations from hexane formed needles, m. p. 106—106·5° (Found: C, 62·25; H, 5·85. $C_{26}H_{29}BrO_5$ requires C, 62·3; H, 5·85%), $\nu_{max.}$ 5·85, 6·40, and 6·70 μ, followed by the 9α-*epimer* (as XI), leaflets (from cyclohexane), m. p. 125—125·5° (Found: C, 62·15; H, 5·8%), infrared spectrum very similar to that of the 9β-ester except for absence of strong band at 7·60 μ.

Rechromatography of mother-liquors and intermediate fractions from both the acetates and the *p*-bromobenzoates established that in both cases the ratio of 9β- to 9α-epimer was 4 : 1.

Alkaline hydrolysis of both 9β- and 9α-bromobenzoates, followed by acetylation, gave the corresponding acetates, identified by m. p. and mixed m. p.

5,6,7,7aα,8,9 10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-9-*ols* [β- (as XII) and α- (as XIII) *Epimers*], *and their Esters*.—The saturated ketone (IX) (1·00 g.) was reduced with lithium hydridotri-t-butoxyaluminate in tetrahydrofuran, as described for the unsaturated ketone (VIII). The crude product (1·10 g.) was heated at 50—60° for 2 hr. with *p*-bromobenzoyl chloride (0·85 g.) in pyridine (5·0 ml.). The crude mixture of *p*-bromobenzoates obtained after the usual working-up was chromatographed on alumina (Alcoa; 35 g.) with hexane as solvent and methylene chloride–hexane as eluant, giving first the 9β-p-*bromobenzoate* (as XII), leaflets (from cyclohexane), double m. p. 112—112·5°, 122—123°, $\nu_{max.}$ 5·85 and 6·26 μ

(Found: C, 62·0; H, 6·3; Br, 16·0. $C_{26}H_{31}BrO_5$ requires C, 62·05; H, 6·2; Br, 15·9%), followed by the 9α-*epimer* (as XIII), needles (from cyclohexane), m. p. 126—126·5° (depressed on admixture with the 9β-epimer), $\nu_{max.}$ 5·85, 6·27 μ (Found: C, 62·1; H, 6·1; Br, 15·9%).

Alkaline hydrolysis of the 9β-*p*-bromobenzoate gave the 9β-*alcohol*, leaflets (from cyclohexane) which retained solvent tenaciously; after intensive drying *in vacuo* they had m. p. 103—104° (Found: C, 71·45; H, 8·95. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%). Acetylation of this alcohol with acetic anhydride–pyridine at 100° for 0·5 hr. gave the 9β-*acetate*, prisms (from hexane), m. p. 102—103°, $\nu_{max.}$ 5·81 and 6·26 μ (Found: C, 69·5; H, 8·4. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·25%). The same product was also obtained by catalytic hydrogenation of the unsaturated acetoxy-compound (from X) in methanol with palladium–strontium carbonate and identified by m. p. and mixed m. p.

Catalytic hydrogenation of the unsaturated 9α-acetoxy-compound (from XI) with palladium–strontium carbonate in methanol gave the 9α-*acetate* (as XIII), needles (from cyclohexane), m. p. 125·5—126°, $\nu_{max.}$ 5·82 and 6·26 μ (Found: C, 69·25; H, 8·2%). Alkaline hydrolysis of this gave the 9α-*alcohol* needles (from cyclohexane), m. p. 117·5—118° (Found: C, 71·25; H, 8·7. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%). Acylation of this with *p*-bromobenzoyl chloride in pyridine gave the 9α-*p*-bromobenzoate (as XIII) identified by m. p. and mixed m. p.

Oxidation of the Acetate of Compound (X) *by Selenium Dioxide.*—The unsaturated acetate (2·83 g.) was heated in pyridine (20 ml.) under reflux. Freshly sublimed selenium dioxide (1·20 g.) was added in small portions during 10 hr., together with further portions of pyridine (total 15 ml). The dark suspension was cooled and most of the pyridine removed *in vacuo* below 50°. Ether was added to the residue and the suspension was filtered. The filtrate was washed with ice-cold 5% hydrochloric acid, water, 5% potassium carbonate solution, and again with water and dried ($MgSO_4$). Removal of solvent *in vacuo* below 40° left a residue which was chromatographed in hexane–methylene chloride (4 : 1) on neutral activated alumina (60 g.) above a short column (3 g.) of a 3 : 1 mixture of alumina and precipitated silver.[17] The initial solvent eluted unchanged starting material (1·0 g.), followed by a mixture of (probably) (XVI) (see below) and the acetoxy-diene (XV) (see below) while methylene chloride and chloroform eluted 9β-*acetoxy*-7,7aα,8,9,10,11,12,12aβ-*octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7α-*ol* (XIV) which after recrystallisation from cyclohexane formed needles, m. p. 117·5—118° (Found: C, 67·2; H, 7·45. $C_{21}H_{28}O_6$ requires C, 67·0; H, 7·5%), $\lambda_{max.}$ 259 mμ (ε 11,000), $\lambda_{min.}$ 243 mμ (ε 7100). After rechromatography of mother-liquors and adjacent chromatographic fractions the total yield of this compound was 35% based on unrecovered starting material.

The fractions preceding this product were twice rechromatographed, giving (in order of elution): (a) 9β-*acetoxy*-8,9,10,11,12,12aβ-*hexahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (XV), needles (from hexane), m. p. 102·5—103·5° (Found: C, 70·4; H, 7·25. $C_{21}H_{26}O_5$ requires C, 70·35; H, 7·3%), $\lambda_{max.}$ 303 (ε 9700), $\lambda_{min.}$ 261 mμ (ε 2400), $\nu_{max.}$ 5·80, 6·26, and 6·40 μ; (b) a *substance* [probably (XVI)], which after recrystallisation from hexane had double m. p. 98—98·5° (needles), 104·5—105° (prisms) (Found: C, 67·25; H, 6·8. $C_{21}H_{26}O_6$ requires C, 67·35; H, 7·0%), $\lambda_{max.}$ 226 mμ (ε 29,000), $\nu_{max.}$ 5·80, 5·95, 6·21, and 6·45 μ.

9β - *Acetoxy* - 5,6,7,7aα,8,9,10,11,12aβ - *decahydro* - 1,2,3 - *trimethoxybenzo*[a]*heptalen* - 7α - *ol* (XVII).—The unsaturated acetoxy-alcohol (XIV) (360 mg.) was catalytically hydrogenated in methanol over 4% palladium–strontium carbonate (150 mg.). Usually this hydrogenation succeeded only after shaking with pre-reduced catalyst, filtration, and addition of fresh catalyst. The product was obtained by filtration, removal of solvent, and crystallisation from chloroform–cyclohexane as prisms of the *acetoxy*-7α-*alcohol* (330 mg.), m. p. 116·5—117·5°, depressed on admixture with starting material. The analytical sample had m. p. 120·5—121°, $\nu_{max.}$ 2·80—2·90 (broad), 5·82, and 6·26 μ (Found: C, 66·9; H, 8·0. $C_{21}H_{30}O_6$ requires C, 66·65; H, 8·0%).

9β - *Acetoxy* - 5,6,7,7aα,8,9,10,11,12,12aβ - *decahydro* - 1,2,3 - *trimethoxybenzo*[a]*heptalen* - 7 - *one* (XVIII).—The acetoxy-alcohol (XVII) (400 mg.) was added to the chromic oxide–pyridine complex (from 0·4 g. of chromic oxide and 4 ml. of pyridine) and the mixture left at room temperature overnight. Ether and benzene were added and the suspension was filtered, washed with 5% hydrochloric acid containing ferrous sulphate, then with water, 5% sodium carbonate solution, again with water, and dried ($MgSO_4$). Removal of solvent and crystallisation of the residue from chloroform–cyclohexane gave the *acetoxy-ketone* (356 mg.), m. p. 155—155·5° (Found: C, 67·25; H, 7·65. $C_{21}H_{28}O_6$ requires C, 67·0; H, 7·5%), $\nu_{max.}$ 5·80—5·85s and 6·25 μ.

[17] Fieser and Ourisson, *J. Amer. Chem. Soc.*, 1953, **75**, 4404.

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Hydrolysis of this compound with 5% methanolic potassium hydroxide, followed by re-acetylation of the product, returned the starting material in high yield.

9β - *Acetoxy* - 5,6,7aα,8,9,10,11,12,12aβ - *decahydro* - 1,2,3 - *trimethoxybenzo*[a]*heptalen* - 7β - *ol* (XIX).—The acetoxy-ketone (XVIII) (434 mg.) was added at 0° to a solution of lithium hydridotri-t-butoxyaluminate (1·3 g.) in tetrahydrofuran (15 ml.), and the solution was left at room temperature overnight. Working-up as described for the reduction of the unsaturated ketone (VIII), followed by crystallisation of the product from cyclohexane, gave the *acetoxy*-7β-*alcohol* (374 mg.), m. p. 123·5—124·5° depressed by admixture with the 7α-epimer (Found: C, 67·05; H, 8·05. $C_{21}H_{30}O_6$ requires C, 66·65; H, 8·0%), $\nu_{max.}$ 2·80 (sharp), 5·82, and 6·25 μ.

9β-*Acetoxy*-5,6,8,9,10,11,12,12aβ-*octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (XXa).—(*a*) The acetoxy-7β-alcohol (XIX) (92 mg.) was dissolved in dry pyridine (0·3 ml.), and freshly distilled methanesulphonyl chloride (0·06 ml.) was added at −10°. After being kept overnight at room temperature the red suspension was decomposed with ice, the product was isolated with ether, and the ether layer washed with 5% hydrochloric acid, water, 5% sodium carbonate, again with water, and dried ($MgSO_4$). The ether was removed *in vacuo* at room temperature and the oily residue refluxed under nitrogen with toluene (0·3 ml.) and 2,4,6-trimethylpyridine (0·3 ml.) for 3 hr. Water and ether were added and the ether layer was washed several times with ice-cold 5% hydrochloric acid and water and dried ($MgSO_4$). The residue (88 mg.) obtained on removal of solvent was purified by chromatography on neutral active alumina and crystallisation from pentane to give the unsaturated *acetate* (54 mg.), needles, m. p. 99—99·5° (Found: C, 70·05; H, 7·75. $C_{21}H_{28}O_5$ requires C, 69·95; H, 7·85%), $\nu_{max.}$ 5·81 and 6·25 μ.

(*b*) The acetoxy-7β-alcohol (XIX) (69 mg.) was dissolved in pyridine (0·2 ml.), and phosphorus oxychloride (0·03 ml.) was added. The suspension was heated at 60° for 4 hr., after which it was decomposed with ice. The usual working-up gave a residue which showed a positive Beilstein test. It was still inhomogeneous after chromatography and was separated by fractional crystallisation from pentane into the above unsaturated acetate, m. p. and mixed m. p. 97—99°, and 9β-*acetoxy*-7α-*chloro*-5,6,7,7aα,8,9,10,11,12,12aβ-*decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene*, which after repeated crystallisation from hexane had m. p. 135—136° (Found: Cl, 8·7. $C_{21}H_{29}ClO_5$ requires Cl, 8·95%).

Hydrolysis of the above unsaturated acetate (109 mg.) under reflux in methanol (4 ml.) with 15% sodium hydroxide solution (1·3 ml.) for 15 min. gave 5,6,8,9,10,11,12,12aβ-*octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-9β-*ol* (XXb) (88 mg.), needles (from chloroform–cyclohexane), m. p. 128—128·5° (Found: C, 71·5; H, 8·3. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%).

5,6,8,9,10,11,12,12aβ-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-9-*one* (XXI).—The alcohol (XXb) (70 mg.) was oxidised with the chromic oxide–pyridine complex as described for preparation of the acetoxy-ketone (XVIII), to give the *ketone* (60 mg.), needles (from cyclohexane), m. p. 128·5—129° (Found: C, 71·95; H, 7·75. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·65%), $\nu_{max.}$ 5·90 and 6·25 μ.

9,9 - *Ethylenedioxy* - 5,6,7,7a,8,9,10,11 - *octahydro* - 1,2,3 - *trimethoxybenzo*[a]*heptalene* (cf. XXIII).—The preceding ketone (33 mg.) was heated under reflux with toluene-*p*-sulphonic acid (10 mg.) in acetone (1 ml.) for 1 hr. Removal of the acetone and isolation with ether gave a residue which was absorbed in hexane on active acidic alumina (Woelm; activity I) (1 g.) and eluted with methylene chloride. Removal of solvent from the eluate gave an oil (22 mg.) [probably the ketone (XXIII)] which had $\lambda_{max.}$ 255 mμ (log ε 3·92), $\lambda_{min.}$ 243 mμ (log ε 3·86), $\nu_{max.}$ 5·89, 6·25, 6·40 μ, and a small band at 6·06 μ (trace of αβ-unsaturated ketone). This (20 mg.) was heated in benzene (1·5 ml.) with ethylene glycol (0·06 ml.) and toluene-*p*-sulphonic acid (5 mg.) for 4 hr. under a small condenser containing silica gel. The product obtained after the customary working-up was chromatographed in hexane on alumina (1 g.). The same solvent eluted the *ketal* which after crystallisation from pentane formed prisms (11·5 mg.), m. p. 96·5—97° (Fisher block), $\lambda_{max.}$ 256 mμ (ε 13,500), $\lambda_{min.}$ 240 mμ (ε 9400) [reported [11] for the degradation product from colchicine: m. p. 95—96°; $\lambda_{max.}$ 256 ± 2 mμ (log ε 4·1), $\lambda_{min.}$ 243 ± 2 mμ (log ε 3·95)]. A sample of the above synthetic product was found by Professor Rapoport to be identical with his degradation product by mixed m. p. determination and in infrared spectrum.

This isomerisation was investigated by following the change in the infrared spectrum of the ketone (XXI) in chloroform containing *ca.* 1% of hydrogen chloride. After 6 hr. an inflexion at 6·39 μ developed to a distinct band (styrene double bond); after 24 hr. a small band

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at 6·05 μ (trace of αβ-unsaturated ketone) appeared. The carbonyl band at 5·90 μ remained unchanged throughout.

2,3,4-Trimethoxybenzosuber-5-one (*2′,3′,4′-Trimethoxy-1,2-benzocyclohept-1-en-3-one*) (*Improved Procedure*).[18]—3,4,5-Trimethoxybenzaldehyde (5·0 g.) and methyl crotonate (5·1 g.) were added at room temperature with cooling to a solution of potassium (2·1 g.) in dry t-butyl alcohol (80 ml.). The mixture became orange and a solid separated. After being kept overnight it was acidified with acetic acid and water was added. The oil which separated was extracted with ether; the extract was washed with water and dried ($MgSO_4$) and the ether removed. The remaining oil was dissolved in ethyl acetate and hydrogenated at 55 lb./sq. in. over 5% palladium–barium sulphate. The crude product obtained on filtration and removal of solvent was hydrolysed by refluxing 10% sodium hydroxide solution. The acid obtained after the usual working-up was purified by distillation in a high vacuum and crystallisation from hexane, to give δ-(3,4,5-trimethoxyphenyl)valeric acid (5·6 g.), m. p. 68—69° (reported,[19] m. p. 66—68°).

Cyclisation of this acid (5·5 g.) with polyphosphoric acid, prepared from 85% orthophosphoric acid (42 ml.) and phosphoric oxide (75 g.), at 95° for 0·5 hr., followed by crystallisation of the crude product from methanol gave the *ketone* (3·24 g.), m. p. 100° (reported,[19] m. p. 99—100°), $\nu_{max.}$ 5·95 and 6·26 μ.

Methylation. The ketone (2·25 g.) in benzene (50 ml.) was added to a suspension of dry potassium t-butoxide (from 327 mg. of potassium) in benzene (50 ml.). The alkoxide immediately dissolved giving a red solution. About half of the solvent was distilled off and, after cooling, methyl iodide (14 ml.) was added. The mixture was refluxed overnight, water was added, the organic layer was dried ($MgSO_4$), and the solvent removed. The remaining oil was chromatographed in hexane successively on two columns of active alkaline alumina (Woelm; activity I; 30 g. each), and the products were eluted with methylene chloride–hexane in ascending proportions of the former, giving first *2′,3′,4′-trimethoxy-4,4-dimethyl-* (0·21 g.), needles (from hexane), m. p. 78—79° (Found: C, 69·1; H, 7·9. $C_{16}H_{22}O_4$ requires C, 69·05; H, 7·95%), bands at 5·91 and 6·26 μ, followed by *2′,3′,4′-trimethoxy-4-methyl-1,2-benzocyclohept-1-en-4-one* (1·09 g.), prisms (from hexane), m. p. 90—90·5: (Found: C, 67·95; H, 7·45. $C_{15}H_{20}O_4$ requires C, 68·15; H, 7·65%), $\nu_{max.}$ 5·91, 6·26 μ, and finally by unchanged starting ketone (0·61 g.).

2′,3′,4′-Trimethoxy-3-methyl-1,2-benzocyclohepta-1,3-diene (XXVIIIb).—2′,3′,4′-Trimethoxy-1,2-benzocyclohept-1-en-3-one (500 mg.) was added in benzene (5 ml.) to a solution of methylmagnesium iodide, prepared from magnesium (100 mg.) and methyl iodide (0·9 ml.) in ether (10 ml.). After 5 hours' heating under reflux the mixture was worked up in the usual manner, a small amount of phenolic material being removed by extraction with sodium hydroxide solution. The crude product was refluxed in benzene (20 ml.) with naphthalene-2-sulphonic acid (30 mg.) until azeotropic removal of water was complete. The crude oily product from this dehydration was passed in hexane through alumina and distilled at *ca.* $110°/10^{-2}$ mm., to give the oily colourless *product* which crystallised at 0° (Found: C, 72·45; H, 8·05. $C_{15}H_{20}O_3$ requires C, 72·55; H, 8·1%), $\lambda_{max.}$ 248 (ε 9750), $\lambda_{min.}$ 238 mμ (ε 7450), $\nu_{max.}$ 5·95, 6·10 (small), 6·25 and 6·40 μ.

2′,3′,4′-Trimethoxy-3,4-dimethyl-1,2-benzocyclohepta-1,3-diene (XXVIIIc).—The 4-methyl-ketone (500 mg.) was caused to react with methylmagnesium iodide as described above, except that most of the ether was distilled off during the reaction. The crude neutral product was dehydrated and the dehydration product purified as described for (XXVIIIb), giving the *dimethyl derivative* as a slightly coloured oil (Found: C, 73·25; H, 8·45. $C_{16}H_{22}O_3$ requires C, 73·25; H, 8·45%), $\lambda_{max.}$ 251 (ε 10,300), $\lambda_{min.}$ 238 mμ (ε 8100), $\nu_{max.}$ 6·25 and 6·37 μ.

CHEMISTRY DEPARTMENT, ISRAEL INSTITUTE OF TECHNOLOGY,
HAIFA, ISRAEL. [*Received, June 10th*, 1960.]

[18] General method kindly communicated by Dr. A. Dreiding before publication.
[19] Gardner, Horton, Thompson, and Twelves, *J. Amer. Chem. Soc.*, 1952, **74**, 5527.

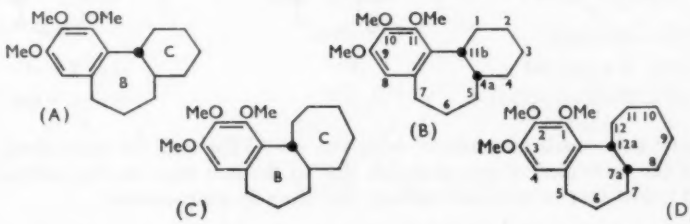
XUM

284. *Syntheses in the Colchicine Series. Part IV.*[1] *Structural and Conformational Aspects in Some Fused Seven-membered Ring Systems.*

By H. J. E. Loewenthal and P. Rona.

The synthesis, constitution, and stereochemistry of a number of compounds containing the ring systems (A), (B), (C), and (D) are discussed, particularly with regard to their bearing on possible conformational analysis in a fused seven-membered ring.

Work described in this and earlier papers [1] involves a number of compounds containing substituents in seven-membered ring systems in which the stereochemistry of the ring junctions has been fairly well established. These compounds offer an opportunity of investigating the conformation of fused seven-membered rings, on which little work has been done in contrast with the effort spent on fused six-membered ring systems.



In this paper we use the prefixes *cis*- and *trans*- always to denote the stereochemistry of the B/C ring-junction (*i.e.*, B and D, or A and C respectively). Asymmetry at other positions is denoted by α or β with reference to the 11b- or 12a-hydrogen atom which is arbitrarily named β. The compounds are, however, all racemates.

The primary object of this work was the synthesis [2] of the tricyclic compound (XIII) which contains the carbon skeleton of colchicine, from which it is obtainable by degradation.[3,4] This synthesis started from 2-(2,3,4-trimethoxyphenyl)cyclohept-1-enecarboxylic acid,[5] whose reduction with lithium in liquid ammonia gave predominantly the *cis*-acid (IVa). The methyl ester of this was largely transformed into that of the accompanying *trans*-acid (Ia) by equilibration with sodium methoxide. The formerly provisional assignment of these configurations is now supported by accumulating evidence [6] that configurational preferences in 1,2-disubstituted cycloheptanes are similar to those obtaining in the corresponding cyclohexanes.

At first this work was continued in the *cis*-series,[2] towards obtaining the system (D) on the basis of previous experience [1] with the model systems (A) and (B). However, later work started mainly from the *trans*-acid (Ia). This was elaborated to the propionic acid (Ic), by the general method described in the preceding paper, that is, through the alcohol (Ib) and its toluene-*p*-sulphonate. Cyclisation of this acid gave the tricyclic *trans*-ketone (II), whose conversion into the olefin (IIIa) also followed the earlier procedures. In the same way the acid (IVa) gave the *cis*-olefin (VIa). As in the preparation of the analogous ketones in the 6,7,6-systems (A) and (B), the conditions of cyclisation of the propionic acids (Ic) and (IVc) to 6,7,7-ring ketones (IIa) and (Va) with polyphosphoric acid had to be carefully studied in order to obtain optimum yields.

Selenium dioxide oxidised the *trans*-olefin (IIIa) in boiling pyridine stereospecifically

[1] Part II, Loewenthal, *J.*, 1958, 1367; Part III, Loewenthal, preceding paper.
[2] Preliminary communication, Loewenthal and Rona, *Proc. Chem. Soc.*, 1958, 114.
[3] Rapoport, Williams, Campion, and Pack, *J. Amer. Chem. Soc.*, 1954, **76**, 3693.
[4] Rapoport, Campion, and Gordon, *J. Amer. Chem. Soc.*, 1955, **77**, 2389.
[5] Boekelheide and Pennington, *J. Amer. Chem. Soc.*, 1952, **74**, 1558.
[6] *E.g.*, Ayres and Raphael, *J.*, 1958, 1779.

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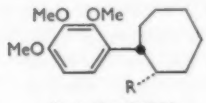
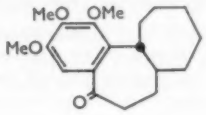
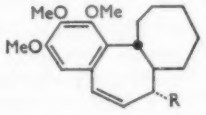
and in reasonable yield to the unsaturated alcohol (IIIb); but similar oxidation of the *cis*-olefin (VIa), even under milder conditions, gave mainly the diene (XX) [which was also obtained by dehydration of the monounsaturated alcohol (IIIb) with dilute acid],



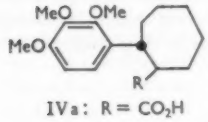
Ia: R = CO_2H
Ib: R = CH_2·OH
Ic: R = $[CH_2]_2$·CO_2H



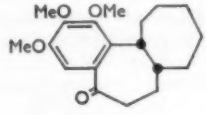
(II)



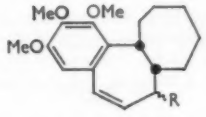
IIIa: R = H
IIIb: R = OH



IVa: R = CO_2H
IVb: R = CH_2·OH
IVc: R = $[CH_2]_2$·CO_2H

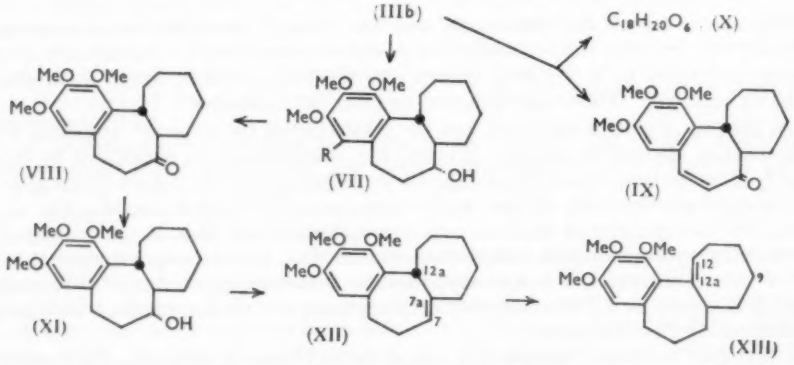


(V)



VIa: R = H
VIb: R = OH

together with very small amounts of both the *cis*- (VIb) and the *trans*-alcohol (IIIb). Isolation of the *trans*-alcohol was probably due to the fact that the low-melting *cis*-acid (IVa) could not at first be obtained entirely free from its *trans*-epimer.



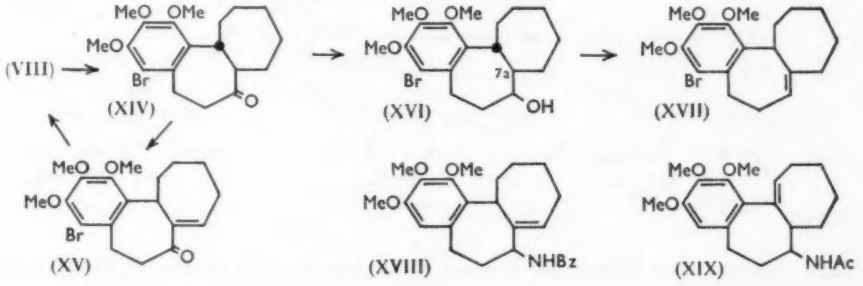
Treatment of the *trans*-alcohol (IIIb) with manganese dioxide gave some of the expected unsaturated ketone (IX), but the main product was a yellow substance, $C_{18}H_{20}O_6$ (*X* in the chart), whose properties are not consistent with retention of the 1,2,3-trimethoxybenzene entity and which is still under examination. A similar compound was obtained under the same conditions from the 9β-acetoxy-analogue (XXXIV) described in the preceding paper

The saturated *trans*-7α-alcohol (VII; R=H) was obtained from the unsaturated alcohol (IIIb) by catalytic hydrogenation and was oxidised to the *trans*-ketone (VIII). This could not be epimerised to a *cis*-epimer under alkaline conditions. Its reduction with lithium hydridotri-t-butoxyaluminate led to the epimeric *trans*-alcohol (XI).

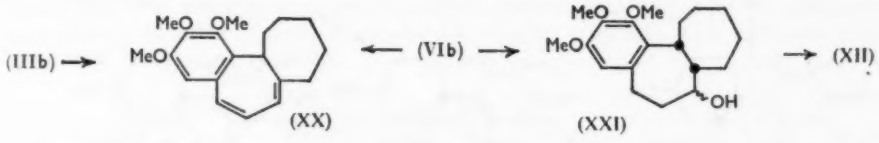
The olefin (XII) was obtained from both the *trans*- (VII; R=H) and the *cis*-alcohol (XXI) by reaction of their toluene-*p*-sulphonates with collidine. With phosphorus oxychloride in pyridine the former alcohol gave a phosphate ester, but the *trans*-7β-epimer (XI) was smoothly dehydrated to the pure olefin (XII). Treatment of this with the boron trifluoride–ether complex in benzene or, preferably, with hydrogen chloride in

chloroform, caused rearrangement to the desired product (XIII), and this was identical with the product obtained when we degraded colchicine by the method described by Rapoport and his co-workers.[4]

The next aim was the synthesis of the colchicine degradation product[3] (XIX). A number of ways were explored to introduce simultaneously the amide group and the styrene double bond. This double bond is known to resist catalytic hydrogenation. Attempts to use the enol acetate of the *trans*-ketone (VIII), by its reaction with peracids or bromine, gave no useful product and will not be described in detail. Bromination of this ketone under buffered conditions gave only the monobromo-ketone (XIV)—the position of the bromine is proved because the aromatic infrared band at 6·26 μ, shown by



all previous compounds in this series, was practically absent. Further bromination of this product in the presence of hydrogen bromide gave an oily dibromo-ketone, in which the position of the carbonyl band in its infrared spectrum was not displaced. Dehydrobromination of this with pyridine or with lithium chloride and lithium carbonate in dimethylformamide[7] led to an unsaturated ketone whose formulation as (XV) is based on the expected αβ-unsaturated carbonyl band at 5·99 μ while the ultraviolet spectrum excluded the presence of a double bond conjugated with the aromatic ring.



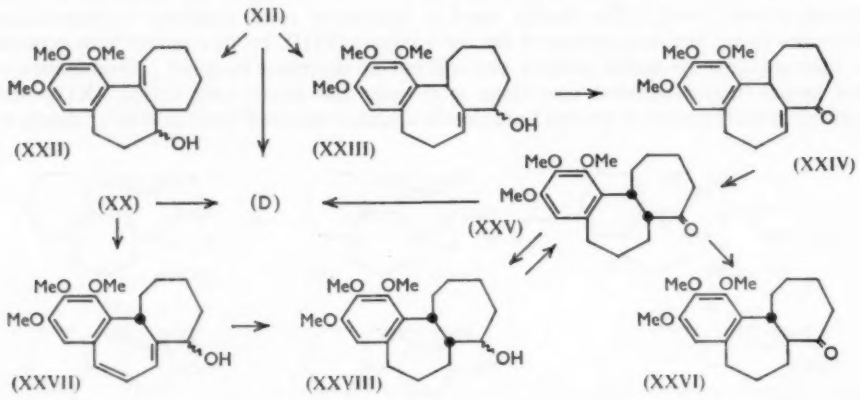
Next the bromo-ketone (XIV) was reduced to the alcohol (XVI), which was smoothly dehydrated to the olefin (XVII). Addition of bromine to the double bond in this, followed by treatment with ammonia and acetylation, appeared to lead to an unsaturated amide. This, however, was clearly not related to the desired compound (XIX), since on catalytic hydrogenation the double bond was reduced before the bromine was removed from the aromatic ring.

Subsequently it was found possible to add bromine to the double bond in compound (XII) without accompanying aromatic bromination. Amination of the resulting dibromide, followed by benzoylation, led to an unsaturated amide in low yield. This again was not related to compound (XIX), on the evidence of its ultraviolet spectrum; it is therefore formulated as (XVIII).

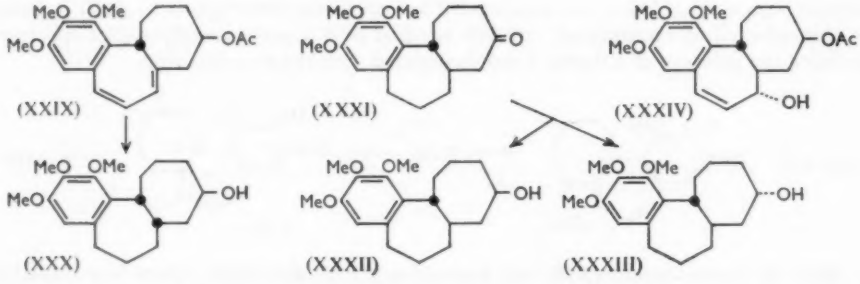
These results, though disappointing, were of value in showing the difficulty of forming a styrene double bond by elimination of a substituent from position 7a under conditions not involving direct protonation. Much the same conclusion was reached on elaboration

[7] Joly, Warnant, Nominé, and Bertin, *Bull. Soc. chim. France*, 1958, 366.

of some products of oxidation of the diene (XX) and the olefin (XII). Treatment of the latter with selenious acid, in a reaction reminiscent of that shown by Δ^7-steroids,[8] gave two unsaturated alcohols, (XXII) and (XXIII). The former showed styrene absorption in its ultraviolet spectrum, but it was obtained in very small yield and could not be



utilised further. The latter was oxidised to an unsaturated ketone (XXIV), whose catalytic hydrogenation gave the ketone (XXV). In this the *cis*-junction between the two seven-membered rings was demonstrated by its conversion, through a thioketal, into the parent *cis*-compound (D). As expected, this ketone was epimerised to the *trans*-ketone (XXVI) by treatment with sodium methoxide.



Oxidation of compound (XX) with selenium dioxide in pyridine gave a single unsaturated alcohol (XXVII) which on catalytic hydrogenation gave the alcohol (XXVIII). This alcohol afforded the previous *cis*-ketone (XXV) and was regenerated from it by reduction with lithium hydridotri-t-butoxyaluminate; with phosphorus oxychloride in pyridine it gave a phosphate.

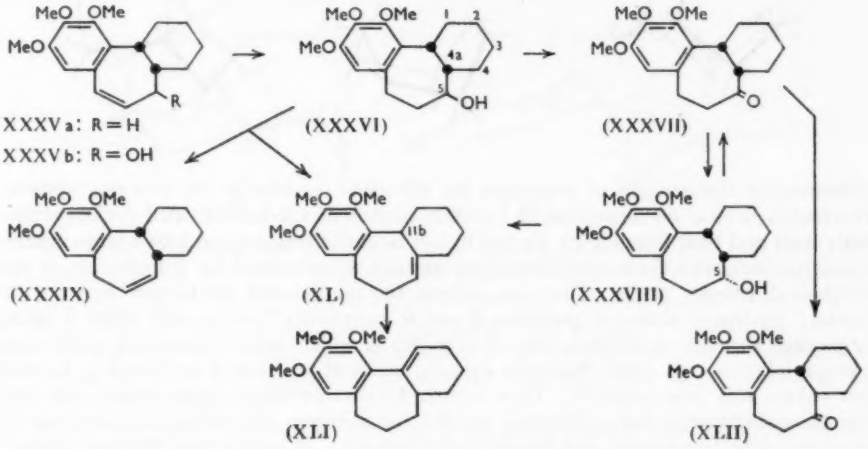
Some further transformations in this series are illustrated in formulæ (XXIX)—(XXXIII). Their significance is discussed below.

Further interesting results were obtained in the *cis*-dibenzo[*a*,*c*]cycloheptatriene system (B). The *trans*-5β-alcohol * (XXXVI), obtained from the unsaturated alcohol [1] (XXXVb), resisted dehydration by phosphorus oxychloride in pyridine, while the 5α-epimer (XXXVIII) obtained by reduction of the *cis*-ketone (XXXVII) afforded the olefin (XL)

* Note the change of numbering for the reduced 6,7,6-ring system.

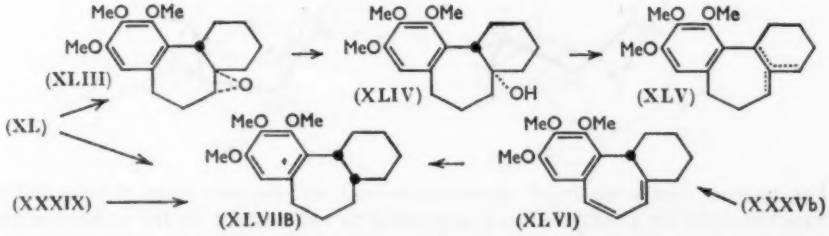
[1] Fieser and Ourisson, *J. Amer. Chem. Soc.*, 1953, **75**, 4404.

under the same conditions. This olefin was obtained also by treatment of the toluene-*p*-sulphonate of the 5β-alcohol (XXXVI) with collidine, but was then contaminated with the isomeric olefin (XXXIX): the mixture was separated by epoxidation which led selectively and stereospecifically to the epoxide (XLIII) and left the 5,6-unsaturated compound (XXXIX) unchanged. This resistance inclined us to formulate the latter



compound as containing a cyclopropane ring in ring B, but that seems to be excluded by the fact that hydrogenation to the *cis*-compound (XLVIIB) is rapid in the presence of palladium–calcium carbonate.

Lithium aluminium hydride reduced the epoxide (XLIII) to a tertiary alcohol (XLIV). Although the hydroxyl group in this compound probably has a conformation favourable for its ionic elimination (see below), dehydration was very difficult. Thionyl chloride in pyridine, or phosphorus oxychloride in the same solvent at 100°, gave a mixture of olefins (XLV) in which only part was of styrene character as judged by the ultraviolet absorption. An attempt to open the epoxide ring by treatment with ammonia under pressure at 120° was unsuccessful.



Stereochemistry.—As discussed by Allinger,[9] the two basic forms of cycloheptane are the chair and the boat form, as in cyclohexane, and here too the chair form appears to be the more stable. An energy difference of 5·5—8·1 kcal./mole between the two forms, calculated by Pauncz and Ginsburg,[10] is of the same order as that (5·3 kcal./mole) found experimentally by Johnson and his co-workers [11] for cyclohexane.

[9] Allinger, *J. Amer. Chem. Soc.*, 1959, **81**, 5727.
[10] Pauncz and Ginsburg, *Tetrahedron*, 1960, **9**, 40.

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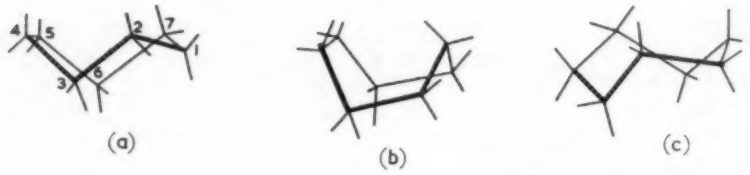
A number of reactions of 1,2-disubstituted cycloheptane derivatives has been studied in connection with the geometric and mechanistic criteria involved, by Sicher and his co-workers [12,13] and by Huffman and Engle.[14] The course of these reactions does not in all cases parallel that exhibited in the cyclohexane series; there may also be considerable

FIG. 1.



differences in the energies of activation for the same reaction in the two ring systems. The reason is clear on inspection of Dreiding models of 1,2-disubstituted cycloheptanes. Both chair and boat forms (Figs. 1a and b) can be easily transformed into a large number of alternatives, and these transformations are not accompanied by deformation of any tetrahedral valency angle. They can release the non-bonded interaction between the "axial" hydrogen atoms at positions 3 and 6, calculated [10] to be only 1·288 Å apart, by passage through an all-skew form [13] (Fig. 1c) in which total transannular interaction is at a minimum. (A slight change in valency angles at positions 4 and 5 in Fig. 1a could also reduce this interaction.[10]) Thus a *trans*-1,2-disubstituted cycloheptane derivative (the two substituents being different) can for the purposes of reaction pass through di-equatorial, equatorial-axial, and diaxial conformations. In such a case there are fourteen possible different chair conformations, of which six allow the two substituents to be both equatorial; and between all three pairs of these there exists an intermediate all-skew form.[15]

The case is somewhat different in cycloheptene, which can also exist in both chair and boat forms. The geometry of these has likewise been evaluated by vector methods [10] (Figs. 2a and b). Both these, especially the chair form, are more rigid than in the case of cycloheptane. Moreover, interaction between the two "axial" 3- and 6-hydrogen atoms is now much less, the separation being about 2·1 Å. Further, a small energy difference in favour of the boat form (0·67 kcal./mole) seems to be indicated.

FIG. 2.

For systems containing fused cycloheptane and cycloheptene rings the possibilities of transformation are greatly reduced, depending to some extent on the stereochemistry of ring fusion (*cis* or *trans*). Indeed the great number of stereoselective reactions revealed in this work makes the presence of a rigid system imperative.

All the compounds described in our work contain a cycloheptene ring (B). Figs. 2a and b show that suitable geometry for, *e.g.*, *trans*-diaxial elimination is found only between

[11] Johnson, Margrave, Bauer, Frisch, Dreger, and Hubbard, *J. Amer. Chem. Soc.*, 1960, **82**, 1255.
[12] Sicher and Svoboda, *Coll. Czech. Chem. Comm.*, 1958, **23**, 2094.
[13] Sicher, Svoboda, Jonas, and Knessl, *Coll. Czech. Chem. Comm.*, 1958, **23**, 2141.
[14] Huffman and Engle, *J. Org. Chem.*, 1959, **24**, 1844.
[15] Cf. Hermans and Maan, *Rec. Trav. chim.*, 1939, **57**, 643.

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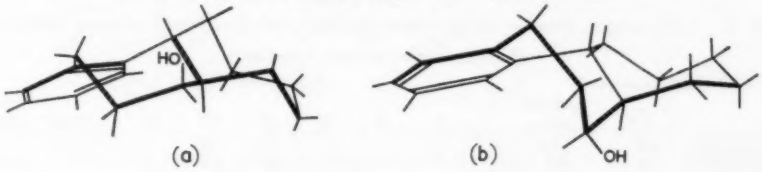
positions 1, 2, and 7. For the ring systems (B) and (C), the ready elimination of water from the alcohols (XXXVIII) and (XI), to give the pure olefins (XL) and (XII) respectively, indicates that the hydroxyl groups and hydrogen atoms involved have a *trans*-diaxial relation. Further, from Figs. 3a and b, 4a and b, it is clear that for such eliminations to be possible ring B has to have a chair conformation in the *trans*-alcohol (XI) and a boat conformation in the *cis*-alcohol (XXXVIII).

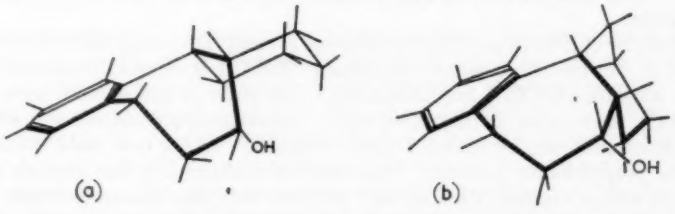
FIG. 3. *Compound* (XI): (a) *ring* B *chair*; (b) *ring* B *boat*.



These " axial " alcohols were prepared by reduction of the ketones (VIII) and (XXXVII) with complex metal hydrides. According to accepted views [16] on the steric course of such reactions, axial alcohols are formed from hindered ketones, while unhindered ketones give equatorial alcohols. Inspection of the interactions in ring B in Figs. 3a and 4a makes it clear that for reagent approach from the *unhindered* side to the *trans*-ketone (VIII) and the *cis*-ketone (XXXVII), quasi-chair and quasi-boat forms must also be assumed in these compounds.

The corresponding " equatorial " alcohols (VII) and (XXXVI) were derived from the " (quasi)equatorial " allylic alcohols (IIIb) and (XXXVb) respectively. These in turn were obtained from the olefins (IIIa) and (XXXVa) by oxidation with selenium dioxide. Not much is known about the steric course of oxidation with this reagent, since in most cases the reaction proceeds further, giving an unsaturated ketone or a conjugated diene.[17] In this work such further oxidation is probably inhibited by the solvent chosen (pyridine). Rosenblum [18] has obtained an allylic alcohol by oxidation of dicyclopentadiene with selenium dioxide, and this compound was shown by Woodward and Katz [19] to be the less hindered *exo*-epimer. In addition, a total synthesis of santonin [20] has involved formation of a quasi-equatorial unhindered hydroxyl group by allylic oxidation with the same

FIG. 4. *Compound* (XXXVIII): (a) *ring* B *boat*; (b) *ring* B *chair*.



reagent. It is probable that experiments on allylic oxidation by selenium dioxide in rigid systems, such as steroids, under the mild conditions used in the present work will show that the formation of an equatorial hydroxyl group is general. The introduction of an *axial* 4β-hydroxyl group on oxidation of cholesterol [21] by selenium dioxide may possibly involve an intermediate cyclic selenite ester.

[16] Barton, *J.*, 1953, 1026.
[17] Rabjohn, in " Organic Reactions," Wiley, New York, 1949, Vol. V, p. 331.
[18] Rosenblum, *J. Amer. Chem. Soc.*, 1957, **79**, 3179.
[19] Woodward and Katz, *Tetrahedron*, 1959, **5**, 70.
[20] Abe, Harukawa, Ishikawa, Miki, Sumi, and Toga, *J. Amer. Chem. Soc.*, 1956, **78**, 1422.
[21] Rosenheim and Starling, *J.*, 1937, 377.

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The action of phosphorus oxychloride and pyridine on the " equatorial " alcohols (VII) and (XXXVI) gave phosphate esters instead of elimination. This is reminiscent of the behaviour of similarly placed equatorial hydroxyl groups in the steroid series.[22,23] The conformations assigned were confirmed, on analogy with six-membered ring systems, by measuring the relative rates of oxidation of these alcohols, and of saponification of their acetates (see Table). The results are clear-cut and in every way consistent with the above mechanistic arguments.

TABLE 1. *Comparative rates of oxidation of alcohols and of saponification of their acetates.*

(Epimeric pairs grouped together.)

	Oxidation of alcohols		Hydrolysis (%) of acetates							
	k *	half-life (min.)	2	4	8	16	32	64	90 hr.	Probable conformn.
(XXXVIII)	40	0·5				6	12			ax
(XXXVI)	0·5	30				30	51			eq
(XI)	54	3·5						5	7	ax
(VII; R=H)	4·3	44				27	53		82	eq
(XXVIII)	7·1	7·5				21	35		74	?
(XXXIII)	3·3	20	14	30	58					ax
(XXXII)	2·6	26	22	43	73					eq
(XXX)			17	35	61					?

* Values relative to 5α-cholestan-3β-ol, $k = 1$.

The analogy to cyclohexane ring systems holds even when the infrared spectra of these compounds are examined. The C–O stretching region of the alcohols (9—10 μ) is unfortunately obscured by absorption due to the aromatic methoxyl groups, but the corresponding region shown by the acetates of the alcohols (VII), (XXXVI), (XI), and (XXXVIII) exhibits a striking parallel to that reported for equatorial and axial acetoxy-groups in steroids.[24] The first two compounds, both " equatorial " by the above arguments, show a single band at 8·06 μ, while the last two, both " axial," show a series of complex bands between 8·0 and 8·2 μ (measured in CS_2).

The relative configurations assigned in this paper to all the above compounds arise from the convention we have adopted, in placing the 11b-hydrogen atom in ring systems (A) and (B), and the 12a-hydrogen atom in systems (C) and (D) above the plane of the molecule (β). This atom most probably has an axial conformation relative to ring c in all these four systems.

The form of the cycloheptane ring c in systems (C) and (D) is more difficult to evaluate. As described in the preceding paper, the ketone (XXXI) is reduced stereoselectively to the epimeric alcohols (XXXII) and (XXXIII). The ratio in which these were obtained (5·5 : 1) is of the same order as that observed in reduction of unhindered steroid ketones, such as 5α-cholestan-3-one, by complex metal hydrides. In the case cited the equatorial alcohol is the preponderant product. The rates of oxidation of the alcohols (XXXII) and (XXXIII) and of saponification of their acetates were also measured (Table 1). The results are consistent in ascribing equatorial and axial character to these epimers, but they indicate that the difference in hindrance between them is rather small. The infrared spectra of these acetates both show a single band at 8·06 μ, that for the 9α-epimer being somewhat broader. If a chair form is assumed for ring c in these compounds (a boat form is shown by models to introduce an inordinate number of transannular interactions), then possible conformations for this ring are indicated in Figs. 5a, b, and c. The first two are preferable in that they best account for the small difference in hindrance between

[22] Barton and Rosenfelder, *J.*, 1951, 1048.
[23] Crawshaw, Henbest, and Jones, *J.*, 1954, 731.
[24] Cole, " Infrared Spectra of Natural Products," in Zechmeister's, " Progress in the Chemistry of Natural Products," Springer, Vienna, 1956, Vol. XIII, p. 1.

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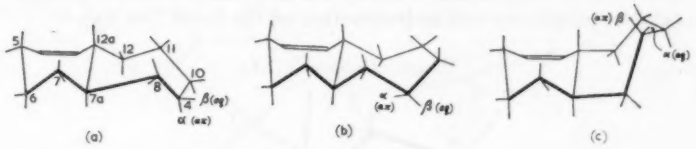
the above two alcohols and their acetates; and on this basis β- and α-configurations have been assigned provisionally. It is intended to clarify this point by establishing a steric relationship between the 7*a*-hydrogen atom and the 9-hydroxyl group in a suitable compound such as the acetoxy-ketone (XVIII) of the preceding paper.

FIG. 5 (*aromatic ring not shown*).



In the *cis*-fused system (D), the shape of the cycloheptane ring C cannot as yet be fully described. Table 1 includes data on alcohols (XXX) and (XXVIII) and their acetates. Unfortunately no epimers of these could be prepared, but the figures might indicate intermediate (equatorial-axial) character for the functional groups. This is reminiscent of results in the flexible *cis*-decalin series,[25] and the flexibility of system (D) is evident from inspection of models.

The stereoselective reduction of the *cis*-ketone (XXV) is somewhat puzzling. If this is hindered, as in ketones (VIII) and XXXVII), then the product (XXVIII) should have an axial 8-hydroxyl group; however, treatment with phosphorus oxychloride–pyridine gave a phosphate ester. *trans*-Diaxial elimination towards $C_{(9)}$ is theoretically possible but would proceed in an anti-Saytzeff direction.

In connection with some current views [26] on the effect of ring size and ring conformation on the infrared spectra of cycloalkanones the wavelengths of the carbonyl bands of the various seven-membered ring ketones encountered in this work have been collected in Table 2. In every case this band was at a lower wavelength for the *trans*- than for the corresponding *cis*-ketone; in the latter one of the rings is probably in the boat form.

TABLE 2. *Infrared carbonyl bands of seven-membered ring ketones.*

(Epimeric pairs grouped together.)

Ketone	(XLII)	(XXXVII)	(VIII)	(XXVI)	(XXV)	(XXXI)	*cis*-Epimer of (XXXI)
Ring junction...	*trans*	*cis*	*trans*	*trans*	*cis*	*trans*	
ν(C:O) (μ)	5·87	5·90	5·90	5·91	5·94	5·90	5·92

Other stereoselective reactions open to interpretation by conformational arguments are the conversion of the olefin (XL) into the epoxide (XLIII), and the reaction of the latter with lithium aluminium hydride which gave a high yield of a tertiary alcohol. Accepted ideas [16] on the stereochemistry of these reductions demand the formation of the axial, and, if possible, the more highly substituted alcohol. When the latter condition is fulfilled, and if the hydroxyl group has a conformation axial to both rings B and C, it must have the α-configuration. This also necessitates an α configuration for the epoxide (XLIII), formed by *rear* attack of a hydroxonium ion on compound (XL); reduction of the ketone (XXXVII) to the alcohol (XXXVIII) must have proceeded by *frontal* attack by the complex-hydride ion. In other words, introduction of the 4a,5-double bond into system (B) has apparently changed the direction of most favourable approach of an ionic reaction species. On the other hand, catalytic reduction of the olefin (XL) proceeded by *frontal* adsorption on the catalyst, giving the *cis*-compound (XLVII). Indeed, catalytic reduction of the similar olefin (XII) and of the dienes (XX), (XXVII), (XXIX), and (XLVI) led in all cases to the formation of the saturated *cis*-fused ring system. We suggest that,

[25] Dauben and Pitzer, in Newman, " Steric Effects in Organic Chemistry," Wiley, New York, 1956, p. 27.

[26] Prelog, *J.*, 1950, 420.

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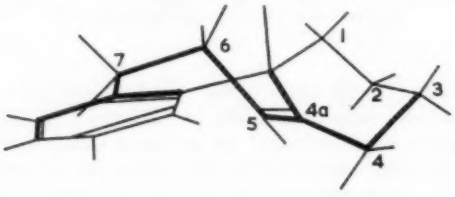
while the direction of approach of an ionic reaction species is determined more by the interactions directly affecting the point of reaction, direction of absorption on a catalyst is governed mainly by the shape of the molecule as a whole.[27] In a relatively flat molecule, such as a steroid, these two factors will in most cases overlap so that catalytic hydrogenation and, *e.g.*, epoxidation will both take place by attack on the same side. In all the above unsaturated compounds, however, the molecule is concave towards the α-side, leading to catalyst adsorption and hydrogenation on the β-side (see Fig. 6).

FIG. 6. *Compound* (XL).



Similar arguments may explain the fact that the chromatographic behaviour of the esters of the alcohol pair (XXXII) and (XXXIII) is the opposite of that expected from the results shown in Table 1, namely, that the equatorial is less strongly absorbed on alumina than the axial epimer (see preceding paper). It has been pointed out[28] that there are exceptions, even in the steroid field, to the rule that compounds containing equatorial functional groups are more strongly absorbed than the axial epimers.

Finally we deal with an item of structural interest, namely, the positions of the double bond that resists hydrogenation in compounds (XIII) and (XLI), which were obtained from the olefins (XII) and (XL), respectively, by protonation, etc. In the 9,9-ethylenedioxy-analogue of compound (XIII) a trisubstituted position (12,12a) for this double bond is almost certain (see preceding paper). In compound (XLI) a similar position is indicated, for this would explain the reluctance of the tertiary hydroxyl group in the alcohol (XLIV) to be eliminated cleanly to give the structure where the double bond is tetrasubstituted. Another argument which could be used is based on conclusions by Henbest and his coworkers[29] on the steric requirements of hydrogen-catalyst migration of double bonds. According to these, such migration may take place if the leaving " allylic " hydrogen atom is sterically accessible to the catalyst surface. If the catalyst, in the present cases, approaches from the β-side, then the 12aβ-hydrogen atom in compound (XII) or the 11b-hydrogen atom in compound (XL) would have the required stereochemistry for such a migration, *provided that* this leads to a compound with a non-hydrogenatable tetrasubstituted double bond. Instead, no migration of the double bond took place and the olefins (XII) and (XL) were hydrogenated to the 7aβ-H and the 4aβ-H compound respectively. A case in point is that of *cis-syn*-1,2,3,4,5,6,12,13,14,15-decahydro-1,1,8-trimethoxy-4-oxochrysene described by Robins and Walker.[30] In this a trisubstituted styrene bond is partly isomerised and partly hydrogenated to give a *cis-syn-cis*-compound, depending on the conditions of the catalytic hydrogenation. Both courses of reaction are compatible with the stereochemistry of the starting material.

If the styrene bond in compounds (XIII) and (XLI) were tetrasubstituted, then it would be contained in a strained cyclohepta-1,3-diene ring in which the two double bonds cannot be in one plane. Moving the double bond to a position exocyclic to that ring would

[27] Cf. Robinson, *Tetrahedron*, 1957, **1**, 49.
[28] Fieser and Fieser, " Steroids," Reinhold Publ. Inc., New York, 1959, p. 698; Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.
[29] Bream, Eaton, and Henbest, *J.*, 1957, 1974.
[30] Robins and Walker, *J.*, 1959, 237.

increase the coplanarity of the conjugated system, and the gain in resonance energy might well offset the loss due to decreased substitution (see Figs. 7a and b).

FIG. 7. *Compound* (XIII).

(a) (b)

Opposed to these conclusions are the results of proton magnetic resonance measurements on compound (XIII), which were kindly undertaken by Drs. Forsen and Nilsson at the Royal Institute of Technology, Stockholm. These provide no positive evidence for the presence of a vinyl proton in ring C of this compound, even though a signal due to this could possibly have overlapped that caused by the lone hydrogen atom in the aromatic ring. We cannot, therefore, at present be certain of the styrene structure shown for these compounds.

EXPERIMENTAL

Infrared spectra are for $CHCl_3$ solutions unless otherwise stated, and ultraviolet spectra for MeOH solutions (Spectrograde).

2-(2,3,4-Trimethoxyphenyl)cycloheptanecarboxylic Acid; trans- (Ia) *and* cis-*Epimers* (IVa).—2-(2,3,4-Trimethoxyphenyl)cyclohept-1-enecarboxylic acid [5] (40 g.) was reduced in liquid ammonia (1300 ml.) with lithium (*ca.* 2 g.) as described previously for the cyclohexane analogue.[1] After isolation with ether–benzene the product was fractionally crystallised from hexane, giving as first crop the trans-*epimer* (10·7 g.) which after recrystallisation had m. p. 96—97° (Found: C, 66·0; H, 7·75. $C_{17}H_{24}O_5$ requires C, 66·2; H, 7·85%). The second crop consisted mainly of the cis-*epimer* (20·0 g.) which after several recrystallisations from hexane had m. p. 74—76° (Found: C, 65·8; H, 7·75%). A third crop (9·0 g.), m. p. 50—70°, also consisted mainly of the *cis*-epimer.

The *cis*-epimer (15·3 g.) was esterified in ether with an excess of diazomethane. The crude methyl ester obtained on removal of solvents *in vacuo* was refluxed with a 15% solution of sodium methoxide in methanol (120 ml.) under nitrogen for 12 hr. Then 10% potassium hydroxide solution (120 ml.) was added, the methanol slowly distilled off, and the remaining solution acidified after cooling. The oil which separated was isolated with benzene and crystallised from hexane, to give the above *trans*-epimer, m. p. and mixed m. p. 95—96° (11 g.). A comparable yield was obtained by subjecting the total epimer mixture obtained from the lithium–liquid ammonia reduction to the same procedure.

trans-*2-(2,3,4-Trimethoxyphenyl)cycloheptylmethanol* (Ib).—This was obtained by reduction of the preceding acid (Ia) (17·8 g.) with lithium aluminium hydride (5·0 g.) in ether–tetrahydrofuran, as described for the cyclohexane analogue.[1] The crude *alcohol* (16·7 g.) was used directly for the next step; a sample was distilled evaporatively at 154—156°/10^{-1} mm. (Found: C, 69·15; H, 8·85. $C_{17}H_{28}O_4$ requires C, 69·35; H, 8·9%), $\nu_{max.}$ at 2·85s, 6·25 μ.

β-trans-*2-(2,3,4-Trimethoxyphenyl)cycloheptylpropionic Acid* (Ic).—The alcohol (Ib) (24·7 g.) was converted into its toluene-*p*-sulphonate ($\nu_{max.}$ 7·35 and 8·51 μ) by treatment with toluene-*p*-sulphonyl chloride (20·35 g.) in pyridine (116 ml.) at 0° overnight (cf. ref. 1). Condensation of this ester with di-t-butyl sodiomalonate (from 45 g. of the malonate and 4·8 g. of sodium hydride) in benzene (120 ml.) and toluene (50 ml.) also followed that described for the cyclohexane analogue. The crude condensation product was heated with acetic acid (400 ml.), water (150 ml.), and concentrated hydrochloric acid (10 ml.) under reflux for 12 hr., after which the solution was concentrated *in vacuo* and the residue heated at 180—200° until gas evolution ceased. It was then dissolved in benzene and extracted several times with 20%

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potassium carbonate solution. The extracts were washed with benzene and acidified, to give the *acid* (20·2 g.) which was isolated with ether–benzene. A sample distilled evaporatively at 190—200°/10^{-1} mm. as a very viscous oil (Found: C, 67·3; H, 8·45. $C_{19}H_{28}O_5$ requires C, 67·85; H, 8·4%).

5,6,7,7aα,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-5-*one* (II).—To the crude acid (Ic) (20·0 g.) was added polyphosphoric acid prepared from 85% orthophosphoric acid (150 ml.) and phosphoric oxide (240 g.), and the reaction mixture was kept at 56—58° with stirring for 25 min. It was then added to ice, and the separated oil was taken up in ether–benzene. The organic layer was washed with 20% potassium carbonate solution and water and dried ($MgSO_4$). Removal of the solvents gave a yellow oil (12·2 g.) from which by crystallisation from pentane at 0° there was obtained a first crop of the *ketone* (6·61 g.) which after further crystallisation from the same solvent had m. p. 80—81° (Found: C, 71·3; H, 8·3. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%), $\nu_{max.}$ 5·92 μ.

Acidification of the alkaline extracts from this reaction gave recovered acid (6·6 g.) which was again cyclised as described above. The neutral portion from this cyclisation (3·6 g.) was combined with the mother-liquors of the first crop of the above ketone, and the whole was chromatographed in hexane on activated alumina (200 g.). Elution with hexane gave a non-ketonic fraction (3·6 g.), followed by the ketone (eluted with methylene chloride) (6·05 g.), making the total yield of ketone 65%.

From this ketone two 2,4-*dinitrophenylhydrazones* were obtained and separated by fractional crystallisation: (*a*) (red), m. p. 198—199° (from cyclohexane) (Found: C, 60·35; H, 6·1; N, 11·25. $C_{25}H_{30}N_4O_7$ requires C, 60·25; H, 6·05; N, 11·25%), and (*b*) (yellow), m. p. 128—129° (from hexane) (Found: C, 60·3; H, 6·15; N, 11·6%).

7,7aα,8,9,10,11,12,12aβ-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (IIIa).—The above ketone (5·48 g.) was reduced with sodium borohydride in methanol, and the resulting alcohol dehydrated with naphthalene-2-sulphonic acid in benzene, by the general procedure described previously.[1] The resulting *olefin* was distilled at 125—130°/10^{-2} mm., to give an oil (4·46 g.) which crystallised; it recrystallised from methanol as needles, m. p. 89—90° (Found: C, 75·95; H, 8·65. $C_{19}H_{28}O_3$ requires C, 75·45; H, 8·65%), $\lambda_{max.}$ 258 mμ (ε 10,800), $\nu_{max.}$ 6·26 and 6·40 μ.

5,6,7,7aα,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (C).—(*a*) The foregoing olefin was catalytically hydrogenated in methanol over 10% palladium–carbon, to give the saturated trans-*compound*, m. p. 86—87° (from methanol) (Found: C, 74·95; H, 9·4. $C_{19}H_{30}O_3$ requires C, 74·95; H, 9·25%), $\lambda_{max.}$ 280 mμ (ε 1050).

(*b*) The ketone (XXXI) (see preceding paper) (140 mg.) was dissolved in ethanedithiol (0·14 ml.) and dioxan (0·3 ml.) in the presence of fused zinc chloride (17 mg.) and anhydrous magnesium sulphate (15 mg.). Next morning water and ether were added and the mixture was worked up in the usual manner. The crude thioketal (125 mg.) was heated in dry ethanol (6 ml.) with Raney nickel (*ca.* 2 g.) under reflux for 3 hr., and the mixture then filtered and evaporated. The residue was extracted several times with hot hexane, and the extracts were filtered, concentrated, and cooled. The product which separated recrystallised from methanol, to give the *trans*-compound, m. p. 86°, undepressed on admixture with the product from experiment (*a*).

7,7aα,8,9,10,11,12,12aβ-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene*-7α-*ol* (IIIb).—To the olefin (IIIa) (4·46 g.) in boiling dry pyridine (30 ml.), selenium dioxide (freshly sublimed; 2·30 g.) was added in small portions during 3 hr., after which heating was continued for another 1·5 hr. The suspension was cooled, diluted with ether–benzene, and filtered. The filtrate was washed with cold 3N-hydrochloric acid, water, 20% potassium carbonate solution, and again water, and dried ($MgSO_4$). Removal of solvents left a dark residue which was chromatographed in methylene chloride–hexane on activated alumina (100 g.) above a short column (4·5 g.) of a mixture of alumina and precipitated silver (1 : 1). Early fractions consisted of unchanged starting material (1·84 g.); after this methylene chloride–chloroform eluted the unsaturated *alcohol* (1·45 g.) which crystallised from cyclohexane in needles, m. p. 154° (Found: C, 71·65; H, 8·15. $C_{19}H_{28}O_4$ requires C, 71·65; H, 8·25%), $\nu_{max.}$ 2·86—2·90 (broad), 6·25 and 6·27 μ. Chromatography of the mother-liquors failed to reveal an epimer.

Oxidation of the Alcohol (IIIb) *with Manganese Dioxide.*—The unsaturated alcohol (0·25 g.) was dissolved in carbon tetrachloride (12 ml.) and active manganese dioxide [21] (3 g.) was added. The suspension was shaken for 8 hr. at room temperature, then filtered, and the manganese

[21] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094.

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dioxide was washed with hot chloroform. The filtrate and washings were combined and the solvents removed. The residue was chromatographed in hexane–methylene chloride (3 : 1) on neutral active alumina. The initial solvent mixture eluted 7,7aα,8,9,10,11,12,12aβ-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7-*one* (IX) (35 mg.), m. p. 87—88° (from pentane) (Found: C, 72·35; H, 7·65. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·65%), $\lambda_{max.}$ 252, 310 mμ (ε 11,300, 10,500), $\nu_{max.}$ 6·02, 6·26, and 6·40 μ. Chloroform eluted a yellow *substance* (X), m. p. 123—124° (from ether) (Found: C, 64·85; H, 6·0; O, 29·0; active H, 0·3. $C_{19}H_{20}O_6$ requires C, 65·05; H, 6·05; O, 28·9; 1H, 0·3%), $\lambda_{max.}$ 266, 351 mμ (ε 36,600, 19,300), $\nu_{max.}$ 6·01—6·10s (broad), 6·23, and 6·34 μ.

8,9,10,11,12,12a-*Hexahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (XX).—The unsaturated alcohol (IIIb) (1.38 g.) was refluxed in ethanol (100 ml.) containing concentrated hydrochloric acid (5 ml.) for 1·5 hr. The solvents were removed *in vacuo* and the residue, isolated with ether–benzene, was purified by chromatography and crystallisation from hexane, giving the *diene* (1·13 g.), m. p. 118—119° (Found: C, 75·65; H, 7·85. $C_{19}H_{24}O_3$ requires C, 75·95; H, 8·05%), $\lambda_{max.}$ 302 mμ (ε 8500), $\nu_{max.}$ 6·25 and 6·37 μ.

Catalytic hydrogenation of this diene (100 mg.) in ethanol in the presence of 10% palladium–carbon (25 mg.) gave in nearly theoretical yield the *cis*-compound (D) (see below), m. p. 86—87°, mixed m. p. 87—89°.

5,6,7,7aα,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7α-*ol* (VII; R=H).—The unsaturated alcohol (IIIb) (0·50 g.) was hydrogenated in methanol over prehydrogenated 5% palladium–calcium carbonate (50 mg.). After the theoretical amount of hydrogen was absorbed (0·5 hr.) the solution was filtered, the solvent removed, and the residue crystallised from cyclohexane, to give the 7α-*alcohol*, m. p. 151—152° (Found: C, 71·7; H, 8·8. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%), $\nu_{max.}$ 2·76 and 6·26 μ. The *acetate*, formed with acetic anhydride–pyridine at 100° (15 min.), had m. p. 106—107° (from pentane) (Found: C, 70·1; H, 8·4. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·35%). The *toluene*-p-*sulphonate*, formed from the alcohol (0·70 g.) and toluene-*p*-sulphonyl chloride (0·60 g.) in pyridine (7 ml.) at 0° overnight, had m. p. 130—131° (from ether–hexane) (Found: C, 65·9; H, 7·55; S, 6·65. $C_{26}H_{34}O_6S$ requires C, 65·8; H, 7·2; S, 6·75%), $\nu_{max.}$ 7·36 and 8·51 μ.

The alcohol (20 mg.), dissolved in dry pyridine (1 ml.), was treated at 0° with phosphorus oxychloride (0·1 ml.), and the mixture was kept for several hours at 0°, then decomposed with ice. Ether was added and the ether layer washed with dilute potassium hydrogen carbonate solution. Evaporation of the dried organic layer gave only a trace of neutral material. Acidification of the alkaline extract followed by isolation with ether gave an oil which showed a strong test for phosphorus on sodium fusion.

5,6,7,7aα,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7-*one* (VIII).—The above 7α-alcohol (0·87 g.), dissolved in dry pyridine (9 ml.), was added to chromic oxide–pyridine complex (from 0·95 g. of the oxide). Next morning benzene–ether was added and the suspension filtered. The filtrate was washed with dilute hydrochloric acid containing 10% of ferrous sulphate, then with water, 20% potassium carbonate solution, and again with water, and dried ($MgSO_4$). Removal of solvents and crystallisation of the residue from hexane gave the *ketone* (0·76 g.), m. p. 109° (Found: C, 71·45; H, 8·4. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%), $\nu_{max.}$ 5·90 μ. The yellow 2,4-*dinitrophenylhydrazone* had m. p. 196—197° (from ethanol–chloroform) (Found: C, 60·35; H, 6·1; N, 11·65. $C_{25}H_{30}N_4O_7$ requires C, 60·25; H, 6·05; N, 11·25%).

Attempted epimerisation of this ketone (180 mg.) with boiling 1% sodium methoxide solution (15 ml.) for 2 hr. led to recovery of starting material, identified by its infrared spectrum and mixed m. p.

β-cis-2-(2,3,4-*Trimethoxyphenyl*)*cycloheptylpropionic Acid* (IVc).—This was prepared, starting from the acid (IVa), in the same was as the *trans*-acid (Ic), through the intermediate cis-2-(2,3,4-*trimethoxyphenyl*)*cycloheptylmethanol* (IVb) (Found, on an evaporatively distilled sample: C, 69·15; H, 8·85. $C_{17}H_{26}O_4$ requires C, 69·35; H, 8·9%), and in comparable yield. The cis-*acid* (IVc) distilled evaporatively at 190—200°/10^{-1} mm. as a very viscous oil (Found: C, 67·3; H, 8·45. $C_{19}H_{28}O_5$ requires C, 67·85; H, 8·4%).

5,6,7,7aβ,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-5-*one* (V).—The *cis*-acid (IVc) (13 g.) was cyclised with polyphosphoric acid in the same manner as the *trans*-acid (Ic), except that the temperature during the cyclisation was kept at 65—67°. The neutral product (9·88 g.) was chromatographed in hexane on alumina (200 g.). All fractions shown

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to be homogeneous by infrared spectra were combined and distilled at 169°/0·1 mm., giving the cis-*ketone* (8·4 g.) as an oil (Found: C, 71·15; H, 8·25. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%), $\nu_{max.}$ 5·96 μ. From this ketone two 2,4-*dinitrophenylhydrazones* were obtained: (*a*) (red), m. p. 200—201° (from cyclohexane) (Found: C, 60·2; H, 6·15; N, 11·25. $C_{25}H_{30}N_4O_7$ requires C, 60·2; H, 6·2; N, 11·2%), and (*b*) (yellow), m. p. 174° (from benzene–cyclohexane) (Found: N, 11·25%).

7,7aβ,8,9,10,11,12,12aβ-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (VIa).—The above *cis*-ketone (8·84 g.) was reduced with sodium borohydride, and the product dehydrated, as indicated for the *trans*-ketone (IIa), to the cis-*olefin* which distilled at 163°/10^{-1} mm. (7·0 g.) and had m. p. 74·5—75° (from pentane at −20°) (Found: C, 75·2; H, 8·7. $C_{19}H_{26}O_3$ requires C, 75·45; H, 8·65%), $\lambda_{max.}$ 262 mμ (ε 14,000), $\nu_{max.}$ 6·26 and 6·40 μ.

Catalytic hydrogenation of this gave 5,6,7,7aβ,8,9,10,11,12,12aβ-*decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (D), m. p. 88—89° (from methanol), strongly depressed on admixture with the *trans*-compound (C) (Found: C, 74·6; H, 9·4. $C_{19}H_{28}O_3$ requires C, 74·95; H, 9·25%).

Oxidation of Compound (VIa) *with Selenium Dioxide.*—To the olefin (7·3 g.) in pyridine (40 ml.) at 85—90°, freshly sublimed selenium dioxide (3·3 g.) was added, with stirring, in small portions during 12 hr. After working up as described for the analogous oxidation of (IIIa) the crude product was chromatographed in hexane on active alumina (140 g.). Elution with hexane gave the diene (XX) (3·7 g.), identified by m. p. and mixed m. p. Chloroform–methylene chloride eluted a mixture of alcohols which were fractionally crystallised from hexane. The first crop, m. p. 150—151° (0·15 g.), was identified with the *trans*-unsaturated alcohol (IIIb) by m. p. and mixed m. p. From the mother-liquor 7,7aβ,8,9,10,11,12,12aβ-*octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7ξ-*ol* (VIb) (0·49 g.) was obtained, with m. p. 110—111° (from hexane) (Found: C, 71·5; H, 8·2. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%).

5,6,7,7aβ,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7ξ-*ol* (XXI).—This *alcohol* was obtained by catalytic hydrogenation of the *cis*-unsaturated alcohol (VIb) in methanol with 5% palladium–calcium carbonate; it had m. p. 138—139° (from hexane) (Found: C, 71·2; H, 9·1. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%), $\nu_{max.}$ 2·79—2·90 (broad) and 6·26 μ.

5,6,7,7aα,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7β-*ol* (XI).—The ketone (VIII) (1·05 g.) was dissolved in dry tetrahydrofuran (40 ml.) and lithium hydridotri-t-butoxyaluminate (3·0 g.) was added. The solution was left at room temperature overnight, after which acetone (5 ml.) was added and most of the solvents were then removed *in vacuo* at room temperature. Water was added; the crude product was isolated with ether–benzene and crystallised from pentane, to give the 7β-*alcohol* (0·94 g.), m. p. 105—106° (Found: C, 71·25; H, 8·75. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%). The *acetate*, formed with acetic anhydride–pyridine at 100° in 15 min., had m. p. 94·5—95° (from pentane) (Found: C, 69·85; H, 8·35. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·35%).

The mother-liquors from the alcohol were chromatographed. At first more of the same compound was obtained, but later a small amount of the more strongly absorbed 7α-alcohol (VII) (*ca.* 20 mg.), identified by m. p. and mixed m. p.

5,6,8,9,10,11,12,12a-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (XII).—(*a*) The above 7β-alcohol (0·77 g.) was dissolved in dry pyridine (5·0 ml.), and phosphorus oxychloride (0·8 ml.) was added at 0°. The mixture was kept at room temperature for 3 hr. and then decomposed by ice. The product was extracted with ether–benzene, washed with dilute hydrochloric acid, water, dilute potassium carbonate solution, and again water, and dried ($MgSO_4$). Removal of solvent and crystallisation from methanol gave the *olefin*, m. p. 102—102·5° (Found: C, 75·3; H, 8·7. $C_{19}H_{26}O_3$ requires C, 75·45; H, 8·65%).

(*b*) The toluene-*p*-sulphonate of the 7α-alcohol (VII; R = H) (1·04 g.) was heated in 2,4,6-trimethylpyridine (3·5 ml.) for 1·5 hr. Water and ether–hexane were added; the organic layer was washed with 3N-sulphuric acid and water and dried ($MgSO_4$). The residue obtained on removal of solvents was chromatographed in hexane on activated alumina (15 ml.). Elution with hexane and hexane–methylene chloride gave the (impure) olefin (0·43 g.), m. p. 90—92° (from methanol), raised on admixture with the product described under (*a*).

(*c*) The *cis*-alcohol (XXI) (0·16 g.) was treated in pyridine (1·5 ml.) with toluene-*p*-sulphonyl chloride (0·11 g.) at 0° overnight. The usual working-up gave an oil which was refluxed with 2,4,6-trimethylpyridine (1 ml.) for 1 hr. Working up as under (*b*) gave the (impure) olefin (0·06 g.), m. p. 95—97°, raised on admixture with the product described under (*a*).

Catalytic hydrogenation of the olefin obtained as under (*a*) (50 mg.) in acetic acid in the

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presence of platinum oxide (10 mg.) gave in practically theoretical yield the *cis*-compound (D), m. p. 85—86°, mixed m. p. 88—89°.

5,6,7,7a,8,9,10,11-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (XIII) (*Deacetamidotetrahydrodemethoxydeoxocolchicine*).—(*a*) Colchicine was degraded as described by Rapoport *et al.*[4] The product had m. p. 76—77° (lit.,[4] 76·4—77·5°).

(*b*) A solution of the olefin (XII) (100 mg.; m. p. 95—97°) in chloroform (4 ml.) was saturated with dry hydrogen chloride at −10° and left at this temperature overnight. The chloroform was then removed *in vacuo* and the residue crystallised from methanol to give the olefin (XIII), m. p. 72—74° (52 mg.). Further crystallisation from methanol gave needles, m. p. 78—78·5°, undepressed on admixture with the degradation product. The infrared spectra of the two compounds (in $CHCl_3$ and CS_2) were identical.

This method gave a purer product than treatment with the boron trifluoride–ether complex in benzene, as previously described.[2]

The synthetic product (20 mg.) with ethereal monoperphthalic acid gave the epoxide, m. p. 116·5° (from hexane) (lit.,[4] m. p. 116—117°).

4 - *Bromo* - 5,6,7,7aα,8,9,10,11,12,12aβ - *decahydro* - 1,2,3 - *trimethoxybenzo*[a]*heptalen* - 7 - *one* (XIV).—To the ketone (VIII) (0·58 g.) and sodium acetate (0·31 g.) in acetic acid (5 ml.) and ether (4 ml.), 0·5M-bromine in acetic acid (4·26 ml.) was added dropwise with stirring at room temperature, and the suspension was stirred for another 0·5 hr. More ether and 5% sodium sulphite solution were added; the organic layer was washed with sodium hydrogen carbonate solution, then with water, and dried ($MgSO_4$) Removal of solvent and crystallisation from pentane gave the *bromo-ketone* (0·62 g.), m. p. 121—122° (Found: C, 57·15; H, 6·25; Br, 20·2. $C_{19}H_{25}BrO_4$ requires C, 57·45; H, 6·35; Br, 20·1%); it showed the ketone band at 5·86 μ, but the aromatic band at 6·25 μ was very weak. The 2,4-*dinitrophenylhydrazone* had m. p. 176° (from ethanol) (Found: N, 9·75; Br, 13·85. $C_{25}H_{29}BrN_4O_7$ requires N, 9·7; Br, 13·85%).

Dehalogenation of this bromo-ketone (44 mg.) by shaking it in hydrogen in methanol (4 ml.) in the presence of pre-reduced 5% palladium–calcium carbonate (20 mg.) gave an oil (31 mg.) which, crystallised from hexane, had m. p. 104—105°, raised on admixture with the ketone (VIII). The infrared spectra were identical.

4 - *Bromo* - 5,6,7,7aα,8,9,10,11,12,12aβ - *decahydro* - 1,2,3 - *trimethoxybenzo*[a]*heptalen* - 7β - *ol* (XVI).—The above bromo-ketone (0·60 g.) was reduced with lithium hydridotri-t-butoxyaluminate in tetrahydrofuran, as described for reduction of the ketone (VIII), giving the 4-*bromo*-7β-*alcohol* (0·49 g.), m. p. 99—100° (from pentane) (Found: C, 57·3; H, 7·1; Br, 20·0. $C_{19}H_{27}BrO_4$ requires C, 57·2; H, 6·8; Br, 20·05%), $\nu_{max.}$ 2·79 μ (sharp).

Treatment of this alcohol (0·35 g.) with phosphorus oxychloride in pyridine at 0° as described for formation of the olefin (XII) from the alcohol (XI) gave a product (0·30 g.) which was chromatographically homogeneous but did not crystallise; it was evidently the bromo-olefin (XVII). The aromatic band at 6·25 μ was absent.

4-*Bromo*-5,6,7,7aα,8,9,10,11,12,12aβ-*decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7α-*ol* (VII; R = Br).—The acetate of the alcohol (VII) (0·24 g.), and sodium acetate (0·11 g.), dissolved in acetic acid (1·75 ml.) and ether (3·4 ml.), were treated dropwise with 0·5M-bromine in acetic acid (1·5 ml.). Working-up as described for the bromo-ketone (XIV) gave an oil which was hydrolysed by boiling 5% methanolic sodium hydroxide (15 ml.) in 15 min. Addition of water and isolation with ether–benzene gave the 4-*bromo*-7α-*alcohol* (0·20 g.), m. p. 90—91° (from ether–pentane) (Found: C, 57·35; H, 6·5; Br, 20·45%).

4-*Bromo*-5,6,7,9,10,11,12,12a-*octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7-*one* (?) (XV).—The bromo-ketone (XIV) (1·09 g.) was dissolved in acetic acid (18 ml.) and ether (15 ml.), and a few drops of hydrogen bromide in acetic acid were added. 0·5M-Bromine in acetic acid (6·4 ml.) was added dropwise with stirring, excess of bromine being avoided. Sodium acetate (0·24 g.) was then added and the solvents were removed *in vacuo* at room temperature. After addition of water the product was taken up in ether–benzene, washed with potassium hydrogen carbonate solution and water, and dried ($MgSO_4$). The residue obtained on removal of solvents *in vacuo* was heated in dry pyridine (6 ml.) at 120—130° during 1·25 hr. After cooling, ether–benzene was added and the organic layer washed with dilute hydrochloric acid and water and dried ($MgSO_4$). The oily product (1·08 g.) was chromatographed in hexane on neutral activated alumina. Elution with methylene chloride and crystallisation from pentane gave the unsaturated *bromo-ketone* (0·46 g.), m. p. 141—142° (Found: C, 57·9; H, 6·1; Br, 20·2. $C_{19}H_{23}O_4Br$ requires C, 57·75; H, 5·85; Br, 20·2%), $\nu_{max.}$ 5·99 (unsaturated ketone), 5·85w,

6·19s μ (no aromatic band at 6·25 or styrene band at 6·40 μ), with no selective absorption in the range 220—300 mμ.

Shaking this bromo-ketone (0·13 g.) under hydrogen in methanol over pre-reduced 5% palladium–calcium carbonate (0·13 g.) gave an oil (0·10 g.) (negative Beilstein test) which after chromatography on active alumina (Woelm; activity I; 2·5 g.) and crystallisation from hexane gave the ketone (VIII), m. p. 103—104°, raised on admixture (correct infrared spectrum).

Oxidation of Compound (XII) *with Selenious Acid.*—To the olefin (0·64 g.), dissolved in ether (21 ml.), acetic acid (17 ml.), and water (3·4 ml.), was added a 0·1N-solution of selenious acid in acetic acid (16·2 ml.). The whole was kept at room temperature for 2 days, after which the precipitate of selenium was filtered off. To the filtrate a 50% solution of potassium hydroxide (60 ml.) was added, with cooling to 0°, and the product was extracted with ether–benzene. The extract was washed, dried ($MgSO_4$), and evaporated. The residue was dissolved in 5% methanolic potassium hydroxide (30 ml.) and left at room temperature overnight. Water was added and the product extracted with ether–benzene. The extract was washed and dried ($MgSO_4$) and the residue obtained on removal of solvents chromatographed in hexane on active alumina (12 mg.) above a short column (1·6 g.) of 1 : 1 alumina–precipitated silver. Hexane eluted the diene (XX) (110 mg.), identified by m. p. and mixed m. p. Methylene chloride, chloroform, and chloroform–methanol (96 : 4) eluted a mixture of alcohols which were separated by fractional crystallisation from ether–hexane, giving (*a*): 5,6,7,7a,8,9,10,11-*hexahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-7ξ-*ol* (XXII) (?) (30 mg.), feathery needles (from hexane), m. p. 160—161° (Found: C, 71·55; H, 8·32. $C_{19}H_{28}O_4$ requires C, 71·65; H, 8·25%), $\lambda_{max.}$ 258 mμ (ε 10,400), $\nu_{max.}$ 2·76 (sharp), 6·25, and 6·39 μ; and (*b*) 5,6,8,9,10,11,12,12aβ-*octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-8ξ-*ol* (XXIII) (120 mg.), prisms (from ether–hexane), m. p. 135—136° (Found: C, 71·5; H, 8·35%), $\lambda_{max.}$ 279 mμ (ε 2500), $\nu_{max.}$ 2·79 and 6·26 μ.

5,6,8,9,10,11,12,12a-*Octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-8-*one* (XXIV).—The unsaturated alcohol (XXIII) (50 mg.) in pyridine (0·5 ml.) was added at 0° to chromic oxide–pyridine complex (from 55 mg. of the oxide and 0·5 ml. of pyridine), and the mixture was left overnight at room temperature. Working up as described for the oxidation of (VII), chromatography, and crystallisation from hexane gave the unsaturated *ketone* (20 mg.), m. p. 128—129° (Found: C, 72·4; H, 7·7. $C_{19}H_{24}O_4$ requires C, 72·4; H, 7·65%), which had no selective absorption at 220—300 mμ, and $\nu_{max.}$ 5·95, 6·15, and 6·25 μ.

8,9,10,11,12,12a-*Hexahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-8ξ-*ol* (XXVII).—The diene (XX) (1·15 g.) was dissolved in pyridine (20 ml.), and selenium dioxide (freshly sublimed, 0·51 g.) was added to the refluxing solution in small portions during 2·5 hr., after which heating was continued for another 2·5 hr. The mixture was worked up as described for the oxidation of compound (IIIa) (see above), and the product chromatographed in hexane on active alumina. After elution of unchanged starting material (0·38 g.) with hexane, methylene chloride–chloroform eluted the unsaturated *alcohol* (0·30 g.) which after crystallisation from ether–hexane and intensive drying had m. p. 130—131° (Found: C, 72·25; H, 7·75. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·56%), $\lambda_{max.}$ 304 mμ (ε 6600), $\nu_{max.}$ at 2·77 (sharp), 6·25, and 6·40 μ.

5,6,7,7aβ,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-8ξ-*ol* (XXVIII).—The alcohol (XXVII) (0·30 g.) was hydrogenated in methanol in the presence of pre-reduced 5% palladium–calcium carbonate (50 mg.). Two mol. of hydrogen were rapidly absorbed, giving, after filtration and removal of solvent, the cis-*alcohol*, which after crystallisation from cyclohexane had double m. p. 118—119°, 125—126° (0·25 g.) (Found: C, 71·2; H, 8·65. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%), $\nu_{max.}$ 2·75 (sharp) and 6·25 μ.

Treatment of this alcohol with phosphorus oxychloride–pyridine as described for the alcohol (VII) led to a phosphate.

The *acetate*, prepared by use of acetic anhydride–pyridine at 100° for 25 min., had m. p. 94·5—95° (from pentane), strongly depressed on admixture with the acetate of alcohol (XI) (Found: C, 69·8; H, 8·45. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·35%).

5,6,7,7aβ,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-8-*one* (XXV).—(*a*) The *cis*-alcohol (XXVIII) (142 mg.) was oxidised with chromic oxide–pyridine complex, and the product worked up as described for the oxidation of compound (VII), chromatographed, and crystallised from ether–hexane, to give the cis-*ketone*, m. p. 130—131° (Found: C, 71·5; H, 8·1. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%), $\nu_{max.}$ 5·94 and 6·25 μ (no band at 6·15 μ). The 2,4-*dinitrophenylhydrazone* had m. p. 215—216° (from ethanol–chloroform) (Found: C, 60·35; H, 6·05; N, 11·45. $C_{25}H_{30}N_4O_7$ requires C, 60·25; H, 6·05; N, 11·25%).

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(*b*) The unsaturated ketone (XXIV) (40 mg.) was catalytically hydrogenated in methanol over 5% palladium–barium sulphate (30 mg.). The product, after filtration, removal of solvent, and crystallisation from hexane, had m. p. 126—127°, raised to 128—129° on admixture with the product obtained as under (*a*), but depressed to 119—120° on admixture with starting material.

Conversion of Ketone (XXV) *into Compound* (D).—The ketone (40 mg.) was dissolved in ethane-1,2-dithiol (0·04 ml.) in the presence of fused zinc chloride (5 mg.) and anhydrous magnesium sulphate (4 mg.). After the mixture had been left overnight at room temperature water was added and the product extracted with chloroform, washed with 15% potassium hydroxide solution and water, and dried ($MgSO_4$). Removal of the solvent left a residue whose infrared spectrum showed no carbonyl band. It was refluxed in ethanol (5 ml.) with Raney nickel (*ca.* 2 g.) for 3 hr. After filtration, the ethanol was removed from the filtrate and the residue dissolved in hot hexane. The hexane solution was filtered, concentrated, and cooled. The product which crystallised (25 mg.) had m. p. 80—82°, raised to 84—85° on admixture with the *cis*-compound (D). Comparison of infrared spectra also confirmed the identity.

Reconversion of Ketone (XXV) *into Alcohol* (XXVIII).—To the ketone (0·20 g.) in dry tetrahydrofuran (4 ml.) was added lithium hydridotri-t-butoxyaluminate (0·30 g.). The mixture was left at room temperature overnight, and acetone (2 ml.) was added, whereafter the working up followed the usual procedure. The product (0·18 g.), after recrystallisation from hexane, had m. p. 119—121°, undepressed on admixture with alcohol (XXVIII). The infrared spectra of the two alcohols and of their acetates were identical.

Epimerisation of Ketone (XXV).—The ketone (74 mg.) was refluxed under nitrogen for 2 hr. with 1% methanolic sodium methoxide (6 ml.). The usual working up gave 5,6,7,7a*α*,8,9,10,11,12,12a*β*-*decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-8-*one* (XXVI), which after crystallisation from hexane had m. p. 149·5—150° (Found: C, 71·85; H, 8·15. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%), $\nu_{max.}$ 5·91 μ.

Addition of Bromine to Compounds (XII) *and* (XVII), *and Amination of the Products.*—(*a*) The olefin (XII) (0·30 g.) in carbon tetrachloride (4 ml.) was treated dropwise during 20 min. with a 0·5M-solution of bromine in the same solvent (1·98 ml.). The mixture was kept at room temperature for 1 hr., water was added, the organic layer was dried ($MgSO_4$), and the solvent removed, giving an oil (0·45 g.) which still showed the aromatic 6·25 μ band in its infrared spectrum. This was dissolved in dioxan (4 ml.), and liquid ammonia (10 ml.) was added. The mixture was left in a sealed tube at room temperature for 18 hr. during which a precipitate of ammonium bromide separated. After removal of the ammonia, ether–benzene was added, and the solution was washed with water and then extracted with 3N-hydrochloric acid (3 × 15 ml.). The acidic extracts were basified with potassium carbonate solution, and the product isolated with ether, as an oil (122 mg.). This was dissolved in dry ether, and pyridine (0·3 ml.) and benzoyl chloride (0·15 ml.) were added. After the mixture had been left overnight at room temperature ice was added and the mixture was worked up in the usual manner. The product was twice chromatographed on hexane, giving eventually 17 mg. of material, m. p. 131—134°, which gave a negative Beilstein test for halogen. This was apparently the *amide* (XVIII) (Found: N, 3·4. $C_{26}H_{31}NO_4$ requires N, 3·3%); it showed no selective ultraviolet absorption (220—300 mμ), and no styrene band at 6·40 μ.

(*b*) The crude bromo-olefin (XVII) (0·14 g.), in carbon tetrachloride (4 ml.), was treated dropwise during 20 min. with a 0·5M-solution of bromine in the same solvent (1·05 ml.). The product was isolated and treated with ammoniacal dioxan under pressure as described above. The basic product from this reaction (116 mg.) was left in pyridine (2 ml.) and acetic anhydride (0·7 ml.) at room temperature overnight. The neutral portion of product was then chromatographed on alumina and eluted with hexane–methylene chloride, giving an oil (77 mg.), showing an amide band at 6·0 μ. This (73 mg.) and dry sodium acetate (21 mg.) were dissolved in acetic anhydride (3 ml.), and the solution catalytically hydrogenated in the presence of 5% palladium–carbon (30 mg.) and platinum oxide (15 mg.). One mol. of hydrogen was absorbed but the oily product (72 mg.) still showed a positive Beilstein test for halogen, showing that only the double bond had been reduced. It (68 mg.) was dissolved in methanol (4 ml.) and shaken under hydrogen with pre-reduced 5% palladium–calcium carbonate (20 mg.), giving after the usual working up a *substance*, presumably the saturated *acetamide* corresponding to (XVIII) (35 mg.), m. p. 158—161° (from ether–hexane) (Found: C, 69·2; H, 8·8; N, 4·0.

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$C_{21}H_{21}O_4N$ requires C, 69·75; H, 8·65; N, 3·9%), $\lambda_{max.}$ 281 mμ (ε 880), amide band at 6·05 μ, Beilstein test for halogen negative.

7-*Acetamido*-5,6,7,7a,8,9,10,11-*octahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene* (XIX) (*hexahydrodemethoxydeoxocolchicine*).—This was prepared by degradation of colchicine as described by Rapoport and his co-workers;[3] it had m. p. 183° (lit.,[3] m. p. 183·5—184°).

9β-*Acetoxy*-5,6,7,7aβ,8,9,10,11,12,12aβ-*decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalene*.—9β-Acetoxy-8,9,10,11,12,12aβ-hexahydro-1,2,3-trimethoxybenzo[*a*]heptalene (XXIX) (see preceding paper) (100 mg.) was catalytically hydrogenated in methanol over pre-reduced 4% palladium–strontium carbonate (13 mg.). Filtration, removal of solvent, and crystallisation of the residue from hexane gave the *acetate* of the *cis*-alcohol (XXX), m. p. 113·5—114° (Found: C, 69·3; H, 8·2. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·35%).

Alkaline hydrolysis of this gave 5,6,7,7aβ,8,9,10,11,12,12aβ-*decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-9β-*ol* (XXX), m. p. 119—119·5° (from cyclohexane) (Found: C, 71·35; H, 8·7. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%).

5,6,7,7aβ,8,9,10,11,12,12aβ-*Decahydro*-1,2,3-*trimethoxybenzo*[a]*heptalen*-9-*one*.—The above alcohol (62 mg.) was oxidised with the chromic oxide–pyridine complex (from 65 mg. of the oxide). The usual working up gave the cis-*ketone*, m. p. 150·5—151° (from hexane) (Found: C, 71·45; H, 8·2. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·25%), $\nu_{max.}$ 5·92 μ.

Oxidation of Compound (XXXIV) *with Manganese Dioxide*.—9β-Acetoxy-7,7aα,8,9,10,11,12,12aβ-octahydro-7α-hydroxybenzo[*a*]heptalene (see preceding paper) (0·13 g.) was shaken in carbon tetrachloride (3 ml.) with active manganese dioxide (1·1 g.), and the mixture worked up as described for the analogous oxidation of compound (IIIb). The product was chromatographed on active alumina (3 g.). Elution with hexane gave a small amount of non-crystalline material, followed by a yellow *substance* (65 mg.), eluted with methylene chloride–chloroform. This had m. p. 150—152° (decomp.) (from isopropyl ether) (Found: C, 61·85; H, 5·65. $C_{20}H_{22}O_8$ requires C, 61·55; H, 5·7%), $\lambda_{max.}$ 263, 351 mμ (ε 36,400, 19,200).

1,2,3,4,4aβ,6,7,11bβ-*Octahydro*-9,10,11-*trimethoxy*-5H-*dibenzo*[a,c]*cycloheptatrien*-5β-*ol* (XXXVI).—1,2,3,4,4aβ,11bβ-Hexahydro-9,10,11-trimethoxy-5*H*-dibenzo[*a*,*c*]cycloheptatrien-5β-ol[1] (1·90 g.) was catalytically hydrogenated in ethanol over 4% palladium–strontium carbonate (220 mg.). Concentration of the filtered solution and crystallisation of the product from cyclohexane gave the saturated 5β-*alcohol*, needles, m. p. 132° (Found: C, 70·6; H, 8·5. $C_{18}H_{26}O_4$ requires C, 70·55; H, 8·55%), $\nu_{max.}$ 2·76—2·90 μ (broad). The *acetate* formed with acetic anhydride–pyridine at room temperature had double m. p. 112—113° (needles), 129° (prisms) (from hexane); crystallisation from methanol gave only the high-melting form (Found: C, 68·85; H, 8·15. $C_{20}H_{28}O_5$ requires C, 68·95; H, 8·1%).

Treatment of the alcohol (1·0 g.) with toluene-*p*-sulphonyl chloride (0·74 g.) in pyridine (4 ml.) at room temperature for 4 hr. gave, after the usual working up, the *toluene*-p-*sulphonate* (1·45 g.), which crystallised from methanol as needles, m. p. 150° (Found: S, 7·0. $C_{25}H_{32}O_6S$ requires S, 6·95%), $\nu_{max.}$ 7·36, 8·51 μ.

Oxidation of the alcohol (120 mg.) with chromic oxide–pyridine complex (from 0·15 g. of the oxide) gave 1,2,3,4,4aβ,6,7,11bβ-octahydro-9,10,11-trimethoxy-5*H*-dibenzo[*a*,*c*]cycloheptatrien-5-one[1] (XXXVII) (80 mg.), m. p. and mixed m. p. 115° (from hexane).

Reaction of the alcohol (0·30 g.) with phosphorus oxychloride (0·3 mg.) in pyridine (3 ml.) at room temperature for 3 hr., followed by addition of ice, ether-extraction, and washing of the ether layer with dilute acid and 10% sodium carbonate solution, gave only traces of neutral material. Acidification of the alkaline extract and ether-extraction gave a semicrystalline product which gave a strong test for phosphorus on sodium fusion.

1,2,3,4,4aβ,6,7,11bβ-*Octahydro*-9,10,11-*trimethoxy*-5H-*dibenzo*[a,c]*cycloheptatrien*-5α-*ol* (XXXVIII).—The ketone (XXXVII) (270 mg.) was refluxed in ether (10 ml.) with lithium aluminium hydride (0·12 g.) for 2 hr. After the usual working up the crude product was crystallised from cyclohexane, to give the 5α-*alcohol* (247 mg.), needles, m. p. 163·5—164° (Found: C, 70·15; H, 8·45. $C_{18}H_{26}O_4$ requires C, 70·55; H, 8·55%), $\nu_{max.}$ 2·78 μ (sharp). The *acetate*, formed by acetic anhydride–pyridine at 100° for 2 hr., crystallised as needles (from cyclohexane), m. p. 161° strongly depressed on admixture with starting material (Found: C, 68·55; H, 8·0. $C_{20}H_{28}O_5$ requires C, 68·95; H, 8·1%). Attempted acetylation at room temperature returned mostly unchanged material.

Oxidation of the alcohol with chromic oxide–pyridine complex returned the ketone (XXXVII), identified by mixed m. p.

XUM

1,2,3,4,6,7-*Hexahydro*-9,10,11-*trimethoxy*-11bH-*dibenzo*[a,c]*cycloheptatriene* (XL).—To the alcohol (XXXVIII) (147 mg.) in pyridine (0·6 ml.) was added phosphorus oxychloride (0·18 ml.) at −10°. The suspension was then kept at room temperature for 3 hr. After decomposition with ice, the product was isolated with ether and crystallised from methanol, to give the *olefin* (90 mg.) as prisms, m. p. 116·5—117° (Found: C, 75·0; H, 8·35. $C_{18}H_{24}O_3$ requires C, 74·85; H, 8·4%), $\lambda_{max.}$ 279 mμ (ε 1070, $\nu_{max.}$ 12·25s μ (in CS_2).

4aα,5α-*Epoxy*-1,2,3,4,4a,6,7,11bβ-*Octahydro*-9,10,11-*trimethoxy*-5H-*dibenzo*[a,c]*cycloheptatriene* (XVIII).—The olefin (XL) (0·73 g.) in chloroform (1 ml.) was treated overnight at 5° with ethereal monoperphthalic acid (0·3 mmole/ml.; 10·0 ml.). The usual working up gave a product which was recrystallised from cyclohexane, to give the *epoxide* (0·65 g.), m. p. 160·5—161·5°. The analytical sample had m. p. 164° (Found: C, 70·85; H, 8·05. $C_{18}H_{24}O_4$ requires C, 71·0; H, 7·95%).

After this epoxide had been heated for 3 hr. at 120° in a sealed tube in dioxan previously saturated at 0° with ammonia, only unchanged starting material, identified by m. p. and mixed m. p., was obtained.

1,2,3,4,4aβ,11bβ-*Hexahydro*-9,10,11-*trimethoxy*-7H-*dibenzo*[a,c]*cycloheptatriene* (XXXIX).—The toluene-*p*-sulphonate of the alcohol (XXXVI) (1·0 g.) was heated under reflux with 2,4,6-trimethylpyridine (5 ml.) for 2 hr. The neutral product, isolated with ether, was once crystallised from methanol, to give a mixture, m. p. 102—105°, whose infrared spectrum (in CS_2) was the sum of those of (XL) and (XXXIX) (see below).

This mixture (0·54 g.) in chloroform (1·0 ml.) was treated with ethereal monoperphthalic acid (0·17 mmole/ml.; 7·15 ml., 15% excess), and the solution was left at 0° for 2 days. The usual working up gave a crude product which was once crystallised from cyclohexane, giving the epoxide (XLIII) (210 mg.), m. p. and mixed m. p. 161—162°. The mother-liquors were evaporated to a gum (330 mg.), which was chromatographed in hexane on active alumina (Fisher; 7 g.). The initial solvent eluted the *olefin* (239 mg.), m. p. 102—103° (from methanol). Recrystallisation from methanol until there was no further change in the fingerprint region of the infrared spectrum (in CS_2, see below) gave needles, m. p. 105—105·5° (Found: C, 74·5; H, 8·8. $C_{18}H_{24}O_3$ requires C, 74·95; H, 8·4%), $\lambda_{max.}$ 279 mμ (ε 1200), no pronounced absorption in 12—13 μ region (in CS_2).

Catalytic hydrogenation of the olefins (XL) and (XXXIX), over platinum in acetic acid, or palladium–calcium carbonate, in methanol gave in both cases and in practically quantitative yield 1,2,3,4,4aβ,6,7,11bβ-octahydro-9,10,11-trimethoxy-5*H*-dibenzo[*a,c*]cycloheptatriene [1] (XLVII), identified by m. p. and mixed m. p.

1,2,3,4a,6,7,11bβ-*Octahydro*-9,10,11-*trimethoxy*-5H-*dibenzo*[a,c]*cycloheptatrien*-4aα-*ol* (XLIV).—The epoxide (XLIII) (0·59 g.) was refluxed with lithium aluminium hydride (0·35 g.) in ether (4 ml.) and tetrahydrofuran (4 ml.) for 7 hr. The product obtained in the usual way crystallised from cyclohexane, giving the tertiary *alcohol* (0·44 g.), m. p. 128·5—129°. The analytical sample (needles from methanol) had m. p. 132—132·5° (Found: C, 70·45; H, 8·6. $C_{18}H_{26}O_4$ requires C, 70·55; H, 8·55%), $\nu_{max.}$ 2·79 μ. This compound was recovered unchanged after treatment with excess of chromic oxide–pyridine complex or acetic anhydride–pyridine for 2 days at room temperature.

2,3,4,4a,6,7-*Hexahydro*-9,10,11-*trimethoxy*-5H-*dibenzo*[a,c]*cycloheptatriene* (XLI).—A solution of the olefin (XL) (0·27 g.) in chloroform (5 ml.) was saturated at −10° with dry hydrogen chloride and left overnight at this temperature. The chloroform was then removed *in vacuo* and the residue distilled at 160° (bath)/10^{-2} mm. The distillate of the isomeric *olefin* crystallised spontaneously; it had m. p. 62—63° (Found: C, 75·1; H, 8·15. $C_{18}H_{24}O_3$ requires C, 74·95; H, 8·4%), $\lambda_{max.}$ 252 (ε 9500), $\lambda_{min.}$ 238 mμ (ε 7600).

Dehydration of the Alcohol (XLIV).—The tertiary alcohol (94 mg.) was heated in pyridine (0·25 ml.) with phosphorus oxychloride (0·10 ml.) at 100° for 1 hr. The customary working up gave a solid which after crystallisation from methanol had m. p. 69—73° unchanged by further crystallisation and sublimation at 65°/10^{-4} mm. (Found: C, 75·1; H, 8·4%), $\lambda_{max.}$ 251 mμ (ε 5550), $\lambda_{min.}$ 244 mμ (ε 5320).

1,2,3,4-*Tetrahydro*-9,10,11-*trimethoxy*-11bH-*dibenzo*[a,c]*cycloheptatriene* (XLVI).—The unsaturated alcohol (XXXV) (65 mg.) was heated under reflux in ethanol containing 3% hydrochloric acid (3 ml.) during 1 hr. The solvents were removed and the residue crystallised from methanol, giving the *diene* as prisms, m. p. 107·5—108° (Found: C, 75·85; H, 7·7. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·75%), $\lambda_{max.}$ 293 (ε 6150), $\lambda_{min.}$ 265 mμ (ε 3650), $\nu_{max.}$ 6·26, 6·45 μ.

XUM

Catalytic hydrogenation of this diene in ethyl acetate in the presence of palladium–strontium carbonate led to the *cis*-compound (XLVII), m. p. and mixed m. p. 99—102°.

Measurement of Relative Oxidation Rates of Alcohols.—These were kindly determined by Professor A. Eschenmoser and Mr. L. Moldovanyi at the Eidgenössische Technische Hochschule, Zurich. The concentrations used were: 6×10^{-4} mole/l. for the alcohols and 8×10^{-4} mole/l. for chromic oxide, in 90·5% acetic acid at 20° ± 1°. The rate constants (see Table 1) were calculated as previously described.[32]

Measurement of Relative Rates of Hydrolysis of Acetates.—The acetate (0·066 mmole) was dissolved in 95% ethanol (3 ml.). To the solution was added N/30-sodium hydroxide in 67% aqueous ethanol (5·00 ml.), and the volume was made up to 10·00 ml. with 95% ethanol. The solution was kept at 25·0° ± 1°, and 1·00 ml. portions were withdrawn at intervals and titrated against 0·01N-hydrochloric acid (phenolphthalein). The results, which were checked against a control solution, are shown in Table 1.

We are indebted to Dr. M. Tischler (Merck, Sharp, and Dohme) for a generous gift of colchicine, to Drs. Forsen and Nilsson for proton magnetic resonance measurements on compound (XIII), to Professor A. Eschenmoser and Mr. L. Moldovanyi for measurements of oxidation rates, and to Professor D. Ginsburg for his interest.

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HAIFA, ISRAEL. [*Received, June 10th,* 1960.]

[32] Schreiber and Eschenmoser, *Helv. Chim. Acta*, 1955, **38**, 1529.

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285. *The Relative Stereochemistry of the Rotenoids.**

By CARL DJERASSI, W. D. OLLIS, and R. C. RUSSELL.

Optical rotatory dispersion studies have shown that six natural rotenoids all have the same absolute configuration at two of their asymmetric centres.

THE rotenoids are a family of natural products whose structures show considerable variety and it is therefore of interest to determine the stereochemical relationship between corresponding asymmetric centres. Eight rotenoids (I—VIII) are known and they have all been isolated in an optically active condition. Deguelin (III), however, has not been isolated in a pure state and the figures given for its specific rotation refer to a concentrate.[1] It is unlikely that tephrosin (12a-hydroxydeguelin) is a true natural product as it is probably produced from deguelin (III) by aerial oxidation.[2]

The structural study of rotenone, sumatrol, deguelin, toxicarol, elliptone, and malaccol has been reviewed,[3,4] and the structures of pachyrrhizone [5] and munduserone [6] have been determined more recently. The structures given for sumatrol (III) and malaccol (VI) are probably correct although the alternative linear C/D/E ring fusion is not excluded. The numbering system which we have adopted for the rotenoids is indicated in the formulæ (I—VI) and we should like to thank Dr. R. S. Cahn and Dr. L. Crombie for this proposal and for their advice.

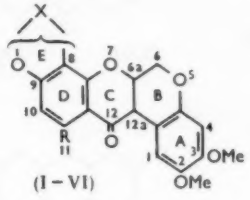
The absolute and relative stereochemistry of the rotenoids has not been defined although it has been subjected to experimental scrutiny.[7,8] The rotenoids (IV—VIII) are racemised

* This paper represents Part XXXVIII in the series by one author (C. D.) and his collaborators on "Optical Rotatory Dispersion Studies" (for Part XXXVII, see R. Villotti, H. J. Ringold, and C. Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 5693).

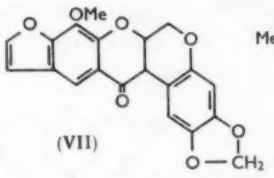
[1] Haller and La Forge, *J. Amer. Chem. Soc.*, 1934, **56**, 2415.
[2] Miyano and Matsui, *Chem. Ber.*, 1959, **92**, 1438.
[3] La Forge, Haller, and Smith, *Chem. Rev.*, 1933, **12**, 182.
[4] Haller, Goodhue, and Jones, *Chem. Rev.*, 1942, **30**, 33.
[5] Bickel and Schmid, *Helv. Chim. Acta*, 1953, **36**, 664.
[6] Finch and Ollis, *Proc. Chem. Soc.*, 1960, 176.
[7] (*a*) Cahn, Phipers, and Boam, *J.*, 1938, 513; (*b*) Jennen, *Bull. Soc. Chim. belges*, 1952, **61**, 536.
[8] Harper, *J.*, 1939, 812.

XUM

under the mild conditions of heating with sodium acetate in ethanol and in the case of munduserone (VIII) it has been established that (±)-munduserone is stereochemically similar to (+)-munduserone.[6] Rotenone under similar conditions gives mutarotenone which is an equilibrium mixture of rotenone and a diastereoisomer; these substances have the same stereochemistry at $C_{(5')}$ but are epimeric at $C_{(6a)}$ and $C_{(12a)}$. These base-catalysed equilibrations involve the anions (IX) and (X),[7b] and Miyano and Matsui[9] have interpreted these results as showing that the B/C ring fusion is *trans*. In our view it is not

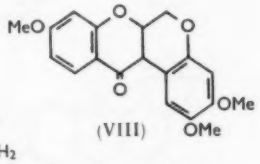


(I – VI)



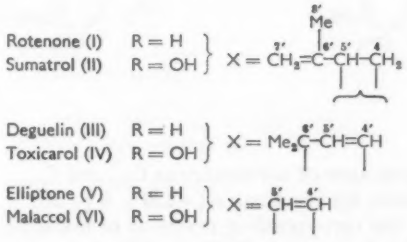
(VII)

Pachyrrhizone (VII)



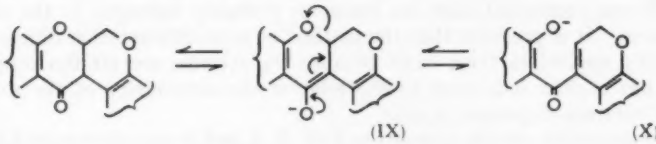
(VIII)

Munduserone (VIII



possible from an examination of models to decide with certainty which is the more stable of the B/C *cis*- and B/C *trans*-arrangements.

At the beginning of our studies the only stereochemical feature which had been established was that the asymmetry at $C_{(6a)}$ and $C_{(12a)}$ in the natural rotenoids was the one which would be associated with greater stability. The stereochemical relation of $C_{(5')}$



(IX) (X)

to $C_{(6a)}$ and $C_{(12a)}$ in rotenone (I) and in sumatrol (II) was not known and it was not established whether the rotenoids all had the same absolute stereochemistry at $C_{(6a)}$ and $C_{(12a)}$.

Compound	I	II	III	IV	V	VI	VII	VIII
$[\alpha]_D$ (Benzene)	−225° [a]	−184° [b]	−101° [a]	−66° [a]	−18° [a]	+67° [a]	0° [c]	—
$[\alpha]_D$ ($CHCl_3$)	−114° [d]	—	—	—	(+55° [c])	+190° [a]	+96° [c]	+103°

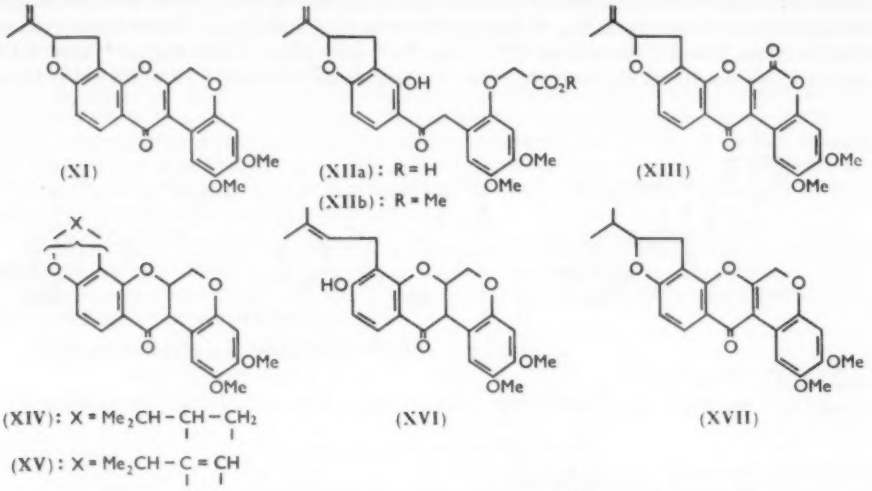
[a] Ref. 10. [b] Ref. 1. [c] Ref. 5. [d] Ref. 11. [e] Ref. 12, in acetone. [f] Ref. 6.

A comparison of the specific rotations (tabulated) did not indicate a stereochemical similarity among the rotenoids so an attempt was made to apply the method of molecular-rotation differences to the problem by determining the optical shifts for three reactions characteristic of rotenoids. The molecular-rotation differences were calculated for reactions

[9] Miyano and Matsui, *Chem. Ber.*, 1958, **91**, 2044.
[10] Harper, *J.*, 1940, 309.
[11] Jones and Smith, *J. Amer. Chem. Soc.*, 1930, **52**, 2554.
[12] Harper, *J.*, 1939, 1099.

XUM

analogous to the following transformations of rotenone: (*a*) rotenone (I) ⟶ dehydrorotenone (XI); (*b*) rotenone (I) ⟶ derrisic acid (XIIa); (*c*) rotenone (I) ⟶ rotenonone (XIII).



These reactions are associated with the disappearance of asymmetry at $C_{(6a)}$ and $C_{(12a)}$, and comparison of the molecular-rotation differences for reactions *a* (+229°), *b* (+202°), and *c* (+247°) for rotenone, with the figures for the corresponding reactions of malaccol (VI) (−699°), pachyrrhizone (VII) (−351°) and munduserone (VIII) (−352°) led us to suspect that the configurations of $C_{(6a)}$ and $C_{(12a)}$ in rotenone were opposite to the configurations of these two centres in malaccol, pachyrrhizone, and munduserone. A similar examination of the specific rotations of the rotenoids has been made by Harper [10] and it was shown by comparison of the pairs of compounds (I and II, III and IV, V and VI) that the introduction of the 11-hydroxyl group gave a positive increment in specific rotation. It was concluded that the rotenoids probably belonged to the same stereochemical series. It is probable that the method of molecular-rotation differences cannot be successfully applied in these cases because the systems are far too conjugated and polarised,* but a clear indication of the relative stereochemistry of the rotenoids was provided by rotatory-dispersion studies.

Rotatory dispersion curves recorded in Figs. 1, 2, and 3 were determined for the compounds listed below.

Rotenone (I) and sumatrol (II) are two naturally occurring rotenoids with an asymmetric centre at $C_{(5')}$ and, as shown in Fig. 1, rotenone and sumatrol acetate exhibit positive Cotton effect curves. Whether the quantitative differences in these two curves can be attributed to the presence of the acetoxy-function *peri* to the carbonyl group in sumatrol acetate or to differences in the configuration at $C_{(5')}$, cannot be decided with the information at present available. Both curves show a negative rotation in the visible range of the spectrum and this feature, of course, explains why their sodium-D line rotations are negative.

In Fig. 2 are collected the rotatory dispersion curves of dehydrorotenone (XI), dehydrodihydrorotenone (XVII), and derrisic acid (XIIa) and its methyl ester (XIIb). These four substances contain only the one asymmetric centre, $C_{(5')}$, and the virtually identical plain negative dispersion curves of these compounds can therefore be ascribed to this

* We thank a Referee for emphasising this point.

sole centre. It is now obvious that the dispersion curves (Fig. 1) of rotenone (I) and sumatrol acetate (cf. II) represent positive Cotton effect curves superimposed upon this negative plain curve and this also applies to the curve of dihydrorotenone (XIV). It is

FIG. 1.

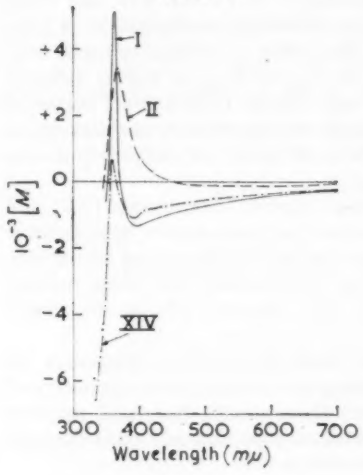


FIG. 2.

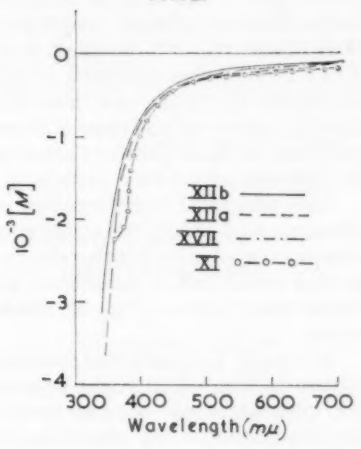


FIG. 3.

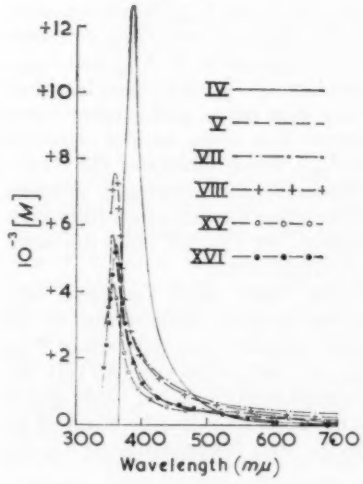


Fig. no.	Substance	Asymmetric centres
1	Rotenone (I)	$C_{(6a)}$ $C_{(12a)}$ $C_{(5')}$
	Sumatrol acetate (cf. II) [7]	,, ,, ,,
	Dihydrorotenone (XIV) [3]	,, ,, ,,
2	Dehydrorotenone (XI) [3]	$C_{(5')}$
	Dehydrodihydrorotenone (XVII) [13]	,,
	Derrisic acid (XIIa) [3]	,,
	Methyl derrisate (XIIb) *	,,
3	Toxicarol (IV) [8]	$C_{(6a)}$ $C_{(12a)}$
	Elliptone (V) [12]	,, ,,
	Pachyrrhizone (VII) [5]	,, ,,
	Munduserone (VIII) [6]	,, ,,
	Rotenonic acid (XVI) [3]	,, ,,
	Isorotenone (XV) [3]	,, ,,

* See p. 1453.

interesting that the amplitude of the Cotton effect of dihydrorotenone (XIV) is considerably smaller than that of rotenone (I) (see Fig. 1). The reason for this is not clear but it is unlikely that this is associated with reduction of the 6′,7′-double bond since this effect is not shown by comparing the dispersion curves of dehydrorotenone (XI) and its 6′,7′-dihydro-derivative (XVII) (see Fig. 2).

Toxicarol (IV), elliptone (V), pachyrrhizone (VII), and munduserone (VIII) all exhibit positive Cotton effect curves (Fig. 3) which are positive throughout the spectral range under examination. These rotenoids lack the asymmetric centre at $C_{(5')}$ and hence are

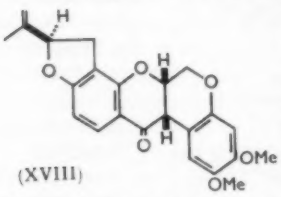
[13] La Forge and Smith, *J. Amer. Chem. Soc.*, 1930, **52**, 1094.

not subject to the initial negative rotational drift in the visible range, as is the case with rotenone (I), where the effect of the positive Cotton effect becomes only noticeable in the ultraviolet region. Since the sign and magnitude of the Cotton effect is associated with the stereochemical environment [14] of the carbonyl chromophore, the positive Cotton effect curves (Figs. 1 and 3) of the naturally occurring rotenoids (I, II, IV, VI, VII, and VIII) can be taken as virtually conclusive evidence of identical absolute configuration at positions 6a and 12a in these substances. The only possible source of ambiguity could arise if two ketones with antipodal absolute configuration at $C_{(6a)}$ or $C_{(12a)}$ *as well as* different ring fusion (*cis* in one case, *trans* in the other) could still exhibit Cotton effect curves of identical sign. At this stage it is not possible to evaluate the significance of quantitative variations in these positive Cotton effect curves as these are partly or completely due to the different substitution patterns in the aromatic ring.

Two additional transformation products of rotenone, namely, isorotenone (XV) and rotenonic acid (XVI), have also been examined. In these two substances, the negative rotatory contribution attributable to $C_{(5')}$ has been removed by the absence of asymmetry at that centre and in accordance with expectation, the two ketones now show positive Cotton effect curves (Fig. 3) which do not start on the negative side in the visible region.

It should be noted that conclusions, based upon molecular-rotation differences for sodium-D light, which might have been drawn regarding the relative stereochemistry of the rotenoids would not necessarily have agreed with these results of optical rotatory dispersion study. The present investigation thus represents a particularly good example of the disadvantage of monochromatic rotation measurements.[15]

Since it has been shown [16] that dihydrodeguelin is identical with β-dihydrorotenone it follows that deguelin (III) has the same configuration at $C_{(6a)}$ and $C_{(12a)}$ as has rotenone. These dispersion measurements demonstrate that all the naturally occurring rotenoids which have been examined possess identical absolute configurations at $C_{(6a)}$ and $C_{(12a)}$, but it is not possible to use the octant rule [17] at the present time to predict what the actual configuration is, owing to the uncertainty about the B/C ring fusion and conformations of rings B and C. It is, however, of considerable interest that seven natural rotenoids all have the same absolute configuration at $C_{(6a)}$ and $C_{(12a)}$, which illustrates the stereoselectivity of their biosynthesis.[18] A similar stereoselectivity also apparently operates in the biosynthesis of flavanoids since those naturally occurring flavans which have been examined and are asymmetric at $C_{(2)}$, all have the same absolute (*R*)-configuration at this centre.[19]



(XVIII)

Note added on 1*st October*, 1960: After this paper was submitted for publication the absolute configuration of the three asymmetric centres of rotenone were determined [20] as (6a*S*, 12a*S*, 5'*R*), giving the full structure (XVIII) for rotenone. This work is complementary to our study and it is now possible to define the absolute stereochemistry of all the rotenoids which we have examined as (6a*S*, 12a*S*). The configuration of $C_{(5')}$ in sumatrol remains to be determined.

Experimental.—All the rotatory dispersion measurements were carried out using dioxan solutions.

[14] Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960.
[15] Ref. 14, pp. 236—237.
[16] Haller and La Forge, *J. Amer. Chem. Soc.*, 1934, **56**, 2417.
[17] Ref. 14, Chapter 13.
[18] Grisebach and Ollis, *Experientia*, 1961, **17**, 4.
[19] Clark-Lewis, "Stereochemistry of Catechins and Related Flavan Derivatives" in "Current Trends in Heterocyclic Chemistry," Ed. A. Albert, G. M. Badger, and C. W. Shoppee, Butterworths, 1958, p. 6.
[20] Büchi, Kaltenbronn, Crombie, Godin, and Whiting, *Proc. Chem. Soc.*, 1960, 274.

XUM

Methyl derrisate (XIIb). Derrisic acid (290 mg.), methanol (10 ml.), and concentrated sulphuric acid (0·2 ml.) were heated under reflux for 5 hr., cooled, and diluted with water. The chloroform extract was washed with aqueous potassium hydrogen carbonate and dried ($MgSO_4$); it yielded *methyl derrisate* (297 mg.) as needles, m. p. 96—97° from methanol [Found: C, 65·25; H, 6·20; OMe, 20·74. $C_{21}H_{17}O_5(OMe)_3$ requires C, 65·15; H, 5·92; OMe, 21·06%].

The botanical sources of the rotenoids are as indicated in the references. We thank Professor H. Schmid, Professor S. H. Harper, and Dr. N. C. Brown for gifts of specimens, Dr. B. F. Burrows and Mr. D. R. George for their assistance with the preparation of some of the compounds studied, and Mrs. T. Nakano for the optical rotatory dispersion measurements.

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(W. D. O. and R. C. R.) The University, Bristol. [*Received, May 27th*, 1960.]

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286. *Co-catalysis. Part II.* The Relative Efficiencies of Halogenated Acetic Acids as Friedel–Crafts Co-catalysts.*

By D. P. N. Satchell.

The rate of loss of carboxylic tritium from acetic, chloroacetic, dichloroacetic, and trifluoroacetic acid to solvent *m*-xylene has been studied, using stannic chloride as catalyst. The general kinetic form is reported, and compared with that observed previously. At the same stannic chloride concentration, and under the simplest kinetic conditions, the order of reactivity is acetic > chloroacetic > dichloroacetic > trifluoroacetic. This result, and previous data, are discussed in relation to Friedel–Crafts co-catalysis. It is concluded that, in the absence of complications due to solvation, the effectiveness of any Brønsted–Lewis acid pair depends primarily on the stability of the complex anion which they form, and this stability, for a given Lewis acid, itself depends on the electron density on that atom of the anion deriving from the Brønsted component, which co-ordinates with the metal.

The diverse reactions which may be broadly defined as of the Friedel–Crafts type include a sub-group whose members require, not only the usual Lewis acid catalyst, but also an additional Brønsted acid co-catalyst. Alkylation with olefins, *cis–trans*-transformation, cationic polymerisation, and electrophilic aromatic substitution by hydrogen are all reactions which, when effected with the aid of Lewis acids, seem on the basis of the present, admittedly restricted, evidence, to require also a co-catalyst whose rôle is to supply protons. Certainly substitution by hydrogen must do so.

As is well known, the immense bulk of Friedel–Crafts literature contains very little systematic quantitative work. Even the comparisons of the various Lewis acids have usually been qualitative, though some general agreement about relative reactivities has been reached.[1] However, the few existing data that bear on the effectiveness of different Brønsted co-catalysts are still contradictory.

Two qualitative studies of this matter have been reported,[2,3] both in connection with cationic polymerisation reactions, and recently we have presented some more quantitative results concerning aromatic hydrogen exchange.[4] We there compared the efficiencies of hydrogen chloride, water, acetic acid, and trifluoroacetic acid as co-catalysts for stannic chloride, in toluene solution. The present report deals with a similar, more detailed, survey of the reactivity of the series of related acids: acetic, chloroacetic, dichloroacetic,

* The paper in *J.*, 1960, 4388, is regarded as Part I.

[1] Baddeley, *Quart. Rev.*, 1954, **8**, 355; Pepper, *ibid.*, 1954, **8**, 88.
[2] Plesch, *Sci. Proc. Roy. Dublin Soc.*, 1950, **25** 154.
[3] Russell, "Cationic Polymerisation and Related Complexes," Heffer, Cambridge, 1953, p. 144.
[4] Part I, Satchell, *J.*, 1960, 4388.

and trifluoroacetic. The results are below compared with conclusions drawn from the polymerisation studies.

Experimental

Materials.—Stannic chloride was purified as previously described.[4] The anhydrous toluene, acetic acid, trifluoroacetic acid, (*carboxy*-^{3}H)acetic acid, and (*carboxy*-^{3}H)trifluoroacetic acid were previous samples.[4] Pure, dry *m*-xylene was prepared by refluxing the Hopkin and Williams product over calcium hydride for several hours before fractionally distilling it. A fraction with b. p. 139·5° was taken. "AnalaR" chloroacetic acid was used as such. [*carboxy*-^{3}H]Chloroacetic acid was prepared by shaking an ether solution of the "AnalaR" acid with tritiated water, separating the phases, and drying and evaporating the ether layer. A final distillation gave a tritiated product, b. p. 189°. Tests [4] showed that probably not more than 2% of the tritium was on the α-carbon atom. Pure dichloroacetic acid and the corresponding anhydride were prepared as previously described.[5] [*carboxy*-^{3}H]Dichloroacetic acid was prepared by addition of a slight deficit of active water to the anhydride. Reaction was rapid at room temperature. Distillation at 0·05 mm. yielded an active product, b. p. 41°. Tests for carbon-bound tritium were not made, but the kinetic experiments, which yielded good plots for tritium loss from this acid, show that contamination of this kind cannot have been serious. Tritiated water was supplied by the Atomic Energy Authority.

General Experimental Arrangements.—These followed the previous pattern and involved a dry-box technique.[4] All experiments were at 25°. Repetitions with different samples of reagents showed the kinetic data to be reproducible and not significantly due to adventitious impurities (*e.g.*, water).

A yellow colour, indicative of complex formation, is present in solutions of stannic chloride in *m*-xylene. The colour intensity decreases with the addition of quantities of the acetic acids. A spectrophotometric analysis of this phenomenon was not attempted in the present work (see Part I).

Radioactive Assay.—This was by a scintillation procedure, previously described.[4]

Results and Discussion

Attention is first drawn to the relative simplicity of the systems here studied as examples of co-catalysed reactions. Only three components are involved: the two acids, and the aromatic hydrocarbon to which tritium is lost by the Brønsted acid. To simplify the exchange kinetics the aromatic compound was used in excess of the other two components, and it could conveniently act as solvent for them. Other types of co-catalysed reaction (*e.g.*, polymerisation) almost always involve an additional, non-reacting component to function as solvent.

Part I dealt with the system HX–$SnCl_4$–toluene, where HX was severally water, acetic acid, trifluoroacetic acid, or hydrogen chloride. Exchange rates, at a given stannic chloride concentration, were in the order hydrogen chloride > water > acetic acid > trifluoroacetic acid. This fact, together with the other kinetic details, led to the general conclusion that it was the ability of the Brønsted acid co-catalyst to form an ionic complex with the Lewis acid which, in the absence of deactivating solvent effects, determined co-catalytic efficiency. It was pointed out that trifluoroacetic acid would be expected to form a stable ionic complex with difficulty, or not at all (there was, however, spectral evidence for some variety of interaction), and the neglible exchange rate found with this co-catalyst was in keeping with the appreciable exchange rate for acetic acid—a compound known to form stable complexes with stannic chloride.[6,7] These two particular results made it appear likely that the series of structurally related acids, acetic, chloroacetic, dichloroacetic, and trichloro(or trifluoro)acetic, would show decreasing co-catalytic activity, in spite of their increasing conventional acid strength. This is the subject now examined.

[5] Satchell, *J.*, 1960, 1752.
[6] Usanovich and Kalabanovskaya, *Zhur. obshchei Khim.*, 1947, **17**, 1235.
[7] Satchell, *J.*, 1958, 3910.

XUM

Some physical evidence,[8] based on viscosity and other data, is held to indicate that, while acetic acid and chloroacetic acid form complexes with stannic chloride, dichloroacetic and trichloroacetic acids do not, or do so only negligibly. One might perhaps, therefore, predict for the series not only decreasing co-catalytic activity, but also a sudden fall in activity when the disubstituted acid is reached; however, this effect is not, in fact, observed (see below).

Some preliminary experiments were conducted in toluene (the aromatic solvent used in the previous work) with chloroacetic acid as co-catalyst. As expected, the observed exchange rate was less than for acetic acid, and in consequence too small for convenient measurement.[4] A change had therefore to be made to a more reactive aromatic compound. Mesitylene proved difficult to purify, different samples giving different colours on the addition of stannic chloride. (The random results obtained by Comyns, Howald, and Willard[9] in experiments with this compound are therefore not thought surprising.) A trial run also showed the exchange rate at quite a low stannic chloride concentration to be very fast. Mesitylene was therefore abandoned.

m-Xylene proved a suitable compound. Purification provided samples giving reproducible kinetic data. The *meta*-isomer was chosen since the others tend to rearrange to it under acidic conditions, and so complication of that kind was avoided. Data obtained for the different acids in exchange with *m*-xylene, at 25°, are tabulated. As will be seen, xylene has a convenient reactivity in the present context. Also the rather small spread of the exchange rates obtained with the four acids enabled it to be used with them all.

The data have two main features: (i) The observed kinetic pattern, common in outline to all the acids. (ii) The relative co-catalytic activity.

(i) *The Kinetic Form.*—This is as previously found for the $CH_3{\cdot}CO_2H$–$SnCl_4$–toluene system.[4] (*a*) There is no observable exchange over long periods in the absence of stannic chloride. (*b*) The exchange rates are in all cases roughly proportional to the stannic chloride concentration. (*c*) At the lowest co-catalyst concentrations the exchange rate is rather little affected by changes in the concentration of this species. (*d*) At higher co-catalyst concentrations (when this species has a concentration comparable with, or greater than, the stannic chloride concentration) the rate falls, though to different extents with the different acids (this effect is discussed below). For a detailed attempt at a mechanistic interpretation of this general kinetic behaviour, see Part I.

TABLE 1. *Exchange between acetic acid and* m-*xylene catalysed by stannic chloride at* 25°.

$[SnCl_4]$	0·086	0·172	0·344	0·344	0·344	0·344
[AcOH]	0·175	0·175	0·175	0·088	0·525	1·85
$10^4\lambda$ (min.$^{-1}$)	28·5	62·2	144	141	126	14·7

In all Tables, λ = first-order exchange rate constant, and square brackets represent molarity.

TABLE 2. *Exchange between chloroacetic acid and* m-*xylene catalysed by stannic chloride at* 25°.

$[SnCl_4]$	0·344	0·344	0·260	0·177	0·177
$[CH_2Cl{\cdot}CO_2H]$	0·053	0·106	0·053	0·053	1·11
$10^4\lambda$ (min.$^{-1}$)	40·6	32·9	27·6	21·0	8·63

TABLE 3. *Exchange between dichloroacetic acid and* m-*xylene catalysed by stannic chloride at* 25°.

$[SnCl_4]$	0·177	0·260	0·344	0·344	0·344	0·344
$[CHCl_2{\cdot}CO_2H]$	0·048	0·048	0·024	0·048	0·288	1·08
$10^4\lambda$ (min.$^{-1}$)	9·6	12·8	21·0	19·3	10·4	6·1

(ii) *Relative Co-catalytic Efficiency.*—Since at co-catalyst concentrations well below that of the stannic chloride, the reaction rate is insensitive to changes in co-catalyst concentration, it seems most legitimate to compare co-catalyst activities in this range. Table 5

[8] Usanovich, Sumarokova, and Glushchenko, *Zhur. obshchei Khim.*, 1951, **21**, 981.
[9] Comyns, Howald, and Willard, *J. Amer. Chem. Soc.*, 1956, **78**, 3989.

XUM

TABLE 4. *Exchange between trifluoroacetic acid and* m-*xylene catalysed by stannic chloride at* 25°.

$[SnCl_4]$	0·34	0·68
$[CF_3{\cdot}CO_2H]$	0·08	0·08
$10^4\lambda$ (min.$^{-1}$)	8·51	17·3

TABLE 5. *Relative rates of exchange at* 0·344M-*stannic chloride for different acids.**

K = acid dissociation constant at 25°.

HX	$10^4\lambda$ (min.$^{-1}$)	K
$CH_3{\cdot}CO_2H$	140	$1{\cdot}8 \times 10^{-5}$
$CH_2Cl{\cdot}CO_2H$	40·6	$1{\cdot}5 \times 10^{-3}$
$CHCl_2{\cdot}CO_2H$	19·3	$5{\cdot}1 \times 10^{-2}$
$CF_3{\cdot}CO_2H$	8·51	>1

* The comparisons are at arbitrary low acid concentrations, the rate being slightly dependent on acid concentration.

contains such a comparison. The catalytic efficiency is seen to be in the order, acetic > chloroacetic > dichloroacetic > trifluoroacetic, with acetic about sixteen times more effective than trifluoroacetic. The observed order is, therefore, as expected, and its qualitative explanation is presumably along the lines previously adumbrated. The co-catalytic process involves, of necessity,[4] the formation of an ionic complex, and the stability of the complex anion will be a determinant of the extent of its own formation. If it is assumed the main determinant, then of the four co-catalysts that possessing the anion which will form the most stable co-ordinate bond with stannic chloride will be the most effective, and that possessing the anion least able to co-ordinate will be the least effective. Thus [4,8] acetic and trifluoroacetic acid would be expected to be the best and worst co-catalyst respectively, as found. This result, in view of their very different conventional acidities, and in the light of a comparison of the protonation equilibria, (i) $B + HX \rightleftharpoons BH^+X^-$ and (ii) $B + HX + SnCl_4 \rightleftharpoons BH^+SnCl_4X^-$ (where B represents the aromatic solvent, and HX the Brønsted component), shows that it must be the satisfaction of the electron-demand of the Lewis acid which plays the dominant rôle in determining complex-formation. Factors which determine the position of equilibrium (i) (which represents the conventional acidity of HX) must be less important.

It will be recalled that, on the basis of the Russian work [8] on the gross physical properties of mixtures of stannic chloride with the chloroacetic acids, a sharp loss of activity after chloroacetic was expected. This is not observed. The relative activities are acetic : chloroacetic : dichloroacetic : trifluoroacetic, 1 : 0·29 : 0·14 : 0·06. Clearly, complex formation must be easier in the exchanging systems than in mixtures of stannic chloride and dichloroacetic acid alone. It is, of course, the presence of the aromatic compound which facilitates complex formation by its solvation, on one way or another, of the acidic hydrogen atoms produced—a rôle dichloroacetic acid itself is presumably little able to play.

The Discussions of this and previous work [4,10] lead to the postulation of a variety of forms for the Brønsted–Lewis complexes, or dual-acids. For Brønsted species such as hydrogen chloride the two most likely forms in solution will be $B \cdots H^{\delta+} \cdots {}^{\delta-}SnCl_5$ and $[BH]^+[SnCl_5]^-$, where B is the solvent. The second, fully ionic complex, being the species which leads directly to reaction (see Part I), will be present in very small amount. Rather similar structures must obtain for acids such as dichloroacetic, discussed above, which themselves solvate their own complexes with difficulty. For acids such as acetic, with greater electron-availability for the anion, the complexes not only require less solvation but may be solvated by the Brønsted component itself. Hence all the following species are probably present in solution: $H_2SnCl_4(OAc)_2$, $[HSnCl_4(OAc)_2]^-[AcOH_2]^+$, $[BH]^+[HSnCl_4(OAc)_2]^-$, together with more highly solvated forms.

[10] Bethell, Gold, and Satchell, *J.*, 1958, 1918.

XUM

As a whole, the exchange experiments indicate that the order hydrogen chloride > water > acetic acid > chloroacetic acid > dichloroacetic acid > trifluoroacetic acid obtains for the effectiveness of the different co-catalysts. The total reactivity spread is a factor of approximately 430. While the mechanisms of catalysis by these acids are undoubtedly different in detail (see Part I, and below) it is probably the stability of the dual-acid anion which, in all cases, determines the extent to which, and thus the rate at which, protons (or tritons) are transferred between the complex acid and the aromatic species. Put another way, the anion stability may be considered to control the extent of formation of the BH^+X^- type of complex, which leads directly to reaction. It is the superficially anomalous position of hydrogen chloride in the reactivity sequence which provides the clue to the fact that it must be the electron density of the co-ordinating atom of the Brønsted acid anion that determines the stability of the complex anion. Thus the chloride ion will have a greater electron density than the oxygen atom of the hydroxide ion, which, in turn, will have a greater electron density than the oxygen atoms of the acetate ion, and so on down the series. This general point will be further supported in Part III.

Comparison with Previous Work.—The results and conclusions outlined above are in some conflict with those obtained from studies of cationic polymerisation. The two relevant investigations, which are qualitative, concern the polymerisation of isobutene at low temperatures, and in an inert medium. With titanium tetrachloride Plesch [2] found water to be a better co-catalyst than acetic, chloroacetic, or dichloroacetic acid, which all, in fact, inhibit polymerisation, while trichloroacetic acid is a satisfactory co-catalyst. A more extended series of Brønsted components was studied by Russell,[3] who used stannic chloride as the Lewis acid. He found activities in the order chloroacetic > acetic > nitroparaffins > water. The position assigned to water differs from that given by Plesch. Nevertheless the general order of effectiveness is that of increasing conventional acidity. This result is not in keeping with that now found for hydrogen exchange, and the conclusions of these authors were correspondingly different. However, the isobutene system very unsatisfactory. During polymerisation co-catalyst is removed, for the anion is involved in chain termination.[11] Clearly if the anions of weak acids are more effective chain-terminators than those of strong acids (as is possible), it would not be surprising that strong acids are better co-catalysts, or that weak acids inhibit the reaction. Moreover, studies of polymerisation in general suffer serious disadvantages from a kinetic viewpoint. They are often conducted at a low temperature (as were the above examples) which exaggerates the problem of contamination by water. The systems are frequently inhomogeneous, and the reaction curves seem often sigmoid. These facts, together with the acknowledged complexity of polymerisation processes, render conclusions about relative co-catalytic efficiency drawn from their study subject to reservation. Many additional, secondary effects may be included in such conclusions. More broadly, the detailed nature of the catalytic process for hydrogen exchange and for polymerisation may differ significantly, for while an essential feature, in each case, will no doubt be the formation, at some stage, of a complex between the Lewis and the Brønsted acid, nevertheless these acids may have other, and different, rôles to play in the two reactions. These other rôles are more likely to be prominent for polymerisation than for exchange.

One of these rôles, played by the Brønsted component, and already mentioned, is common to all co-catalysed systems. As previously mentioned, when the Brønsted acid reaches a concentration comparable with, or greater than, that of the Lewis acid, further increase in Brønsted acid concentration decreases the exchange rate. A similar effect has been observed by Dainton and Tomlinson [12] for the polymerisation of α-methylstyrene by H_2O–$SnCl_4$ in ethyl chloride, and by Eastham [13] for the *cis–trans*-isomerisation of but-2-ene by H_2O–BF_3 in ethyl chloride. Part of the explanation of this effect (see Part I)

[11] Plesch, *J.*, 1950, 543.
[12] Dainton and Tomlinson, *J.*, 1953, 151.
[13] Eastham, *J. Amer. Chem. Soc.*, 1956, **78**, 6040; Eastham and Clayton, *ibid.*, 1957, **79**, 5368.

XUM

for the exchange reactions, and doubtless for other co-catalysed processes also, is that when in excess the Brønsted acid can (further) solvate the complex acid which has been formed (by accepting a proton, or in other ways), and so decrease its tendency to protonate a substrate. Since this feature of co-catalysed reactions is always liable to be present, its isolation is an essential pre-requisite of any kinetic analysis of mechanism.

Different systems will be more or less subject to the phenomenon: as the co-ordinating ability of the Brønsted acid decreases, it should tend to disappear. Some confirmation of this can be discovered by comparing the data in Tables 1 and 2. When a very poorly solvating acid, such as hydrogen chloride, is used, the effect does not noticeably intrude (Part I).

In general, we find that the complexities of Friedel–Crafts co-catalysed systems arise from the varied opportunities for solvation of the reactant species—a conclusion apparently in line with the views of Evans and his collaborators.[14]

KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, August 22nd,* 1960.]

[14] Cf., *e.g.*, Evans and Lewis, *J.*, 1957, 2975.

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287. *Akuamma Alkaloids. Part IV.* The Decomposition of Akuammicine in Methanol.*

By P. N. EDWARDS and G. F. SMITH.

Akuammicine (VII) has been shown to break down to the quaternary pyridinium compound (I) in methanol at 80° and to 3-ethylpyridine and 2-hydroxycarbazole at 140°.

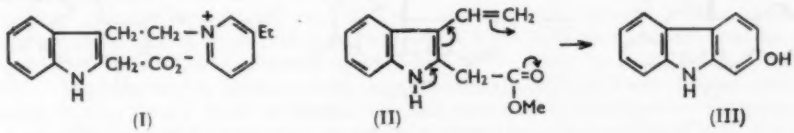
THE identification of ψ-akuammicine with racemic akuammicine led us to explore the possibility of racemisation of akuammicine during the extraction process. To this end, akuammicine was heated in methanol under reflux: very slow decomposition was observed. This decomposition was appreciably faster in a sealed tube at 80°, 30% of the akuammicine being decomposed in 3 hr. The total ether-soluble material from this was shown to be essentially pure akuammicine: on the basis of the molecular weight and $\varepsilon_{330m\mu}$ of akuammicine, the specific rotation of the material in this fraction absorbing at 330 mμ was calculated to be −728°. This shows that no racemisation of akuammicine had occurred. Of the ether-insoluble portion of the reaction, 30% was intractable water- and ether-insoluble tar, and 70% was water-soluble with a well-defined ultraviolet spectrum. This water-soluble material yielded a crystalline betaine, $C_{19}H_{20}N_2O_2$, with complex absorption in the NH and OH stretching region but no C=O band; it formed a picrate $C_{19}H_{20}N_2O_2,C_6H_3N_3O_7$ with bands 3400m (NH), 3300—2300w (diffuse; OH), and 1703s cm.$^{-1}$ (C=O). The ultraviolet spectrum of the betaine is shown in the Figure: the small peak at 290 mμ and the intense peak at 223 mμ strongly suggested an indole nucleus, and the band at 268 mμ, unchanged by acid or alkali, suggested a pyridinium nucleus. In fact the absorption was almost identical with that of an equimolar mixture of 2,3-dimethylindole and β-picoline ethobromide, as shown. On the basis of the known structure of akuammicine (VII) and the above data, the decomposition product has structure (I), and the various salts are quaternary pyridinium salts containing a carboxylic acid group.

Heating akuammicine in methanol to 100° for 3 hr. resulted in 80% decomposition and the isolation of a 70% yield of the picrate of (I), so at this temperature the same decomposition occurs, but much more rapidly.

When akuammicine was heated at 140° in methanol for 2 hr., decomposition was complete, and the only products which could be isolated were 3-ethylpyridine (48%) and 2-hydroxycarbazole (III) (60%). The formation of 3-ethylpyridine follows simply from

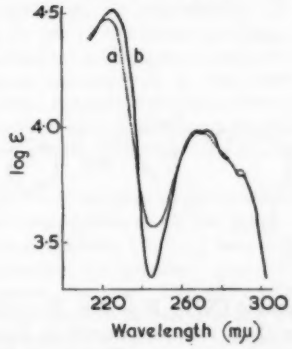
* Part III, Edwards and Smith, *Proc. Chem. Soc.*, 1960, 215.

the methyl ester of (I) (XII; R = Me, X = OMe) (see below). The other immediate product of the elimination should be methyl 3-vinyl-2-indolylacetate (II). This compound was, however, not found. We believe that the 2-hydroxycarbazole (III) is likely to be a transformation product of (II), produced by nucleophilic attack of the vinylogous enamine methylene on the ester-carbonyl carbon, followed by loss of methoxide ion and proton, and by enolisation.



(I) (II) (III)

A number of experiments were carried out in order to throw some light on the very remarkable transformation of akuammicine (VII) into the betaine (I). Akuammicine is completely stable in benzene at 100° and is recovered unchanged after 12 hr.; this suggests



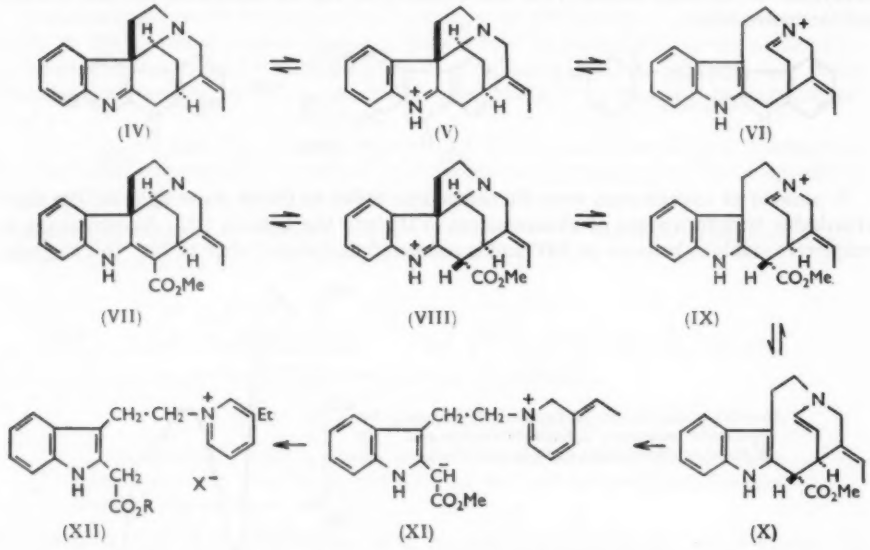
Absorption spectra of: (a) *betaine* (I); (b) *an equimolar mixture of* 2,3-*dimethylindole and* β-*picoline ethobromide* (*both in methanol*).

that the decomposition in methanol may be proton-catalysed. Heating 2,16-dihydroakuammicine in methanol at 100° for 12 hr. leads simply to epimerisation at $C_{(16)}$,[1] the 2,16-double bond therefore plays an essential rôle in the decomposition. Another compound which resists the action of methanol at 100° is akuammicine methiodide. 19,20-Dihydroakuammicine is decomposed in methanol, but much more slowly than akuammicine itself: in methanol at 100° for 5 hr. it is decomposed only to the extent of 10%, and the decomposition product does not contain a pyridinium ion, for it has simple indole absorption in the ultraviolet region; it was not investigated further. About 20% of 19,20-dihydroakuammicine survives being heated in methanol for 3 hr. at 140°; the rest is largely intractable material from which about 10% of 4-ethylpyridine and 10% of 2-hydroxycarbazole can be isolated. This shows that, although the 19,20-double bond is not essential for the decomposition, it greatly facilitates it.

The above results enable us to propose the following sequence of reactions for the overall change of akuammicine into the betaine (I). Bearing in mind the proton-catalysed equilibrium (IV) ⇌ (V) ⇌ (VI), which has been clearly shown to exist in a methanol solution of the product (IV) of acid-hydrolysis of akuammicine, we believe that the first steps in the decomposition of akuammicine are very likely to involve the reversible reactions (VII) ⇌ (VIII) ⇌ (IX). Now if we visualise the further plausible equilibrium involving loss of proton to give the enamine (X), this is nicely constituted to undergo a reverse Michael reaction, by 15,16-bond fission, to give compound (XI). This step may be regarded as irreversible, since it involves the opening of a nine-membered ring. A racemisation of akuammicine to ψ-akuammicine would have to involve the change

[1] Edwards and Smith, *J.*, in the press.

(XI) ⟶ racemic (X), which we regard as highly unlikely. This change would furthermore have to occur more rapidly than aromatisation to the pyridinium system. The final steps are proton addition to the mesomeric carbanion in (XI) and double-bond migration into the pyridine ring. The product expected from this reaction would be the methyl



ester methoxide (XII; R = Me, X = OMe). The fact that the actual product isolated is the betaine (I) is to be explained as saponification due to traces of water in the methanol used, which allows the equilibrium $MeO^- + H_2O \rightleftharpoons MeOH + OH^-$ to be set up.

The crucial step in the decomposition of akuammicine is thus the irreversible 15,16-bond fission (X ⟶ XI). It is extremely likely that the slowing down of the decomposition of 19,20-dihydroakuammicine occurs at the corresponding step: in akuammicine, the 19,20-double bond actually assists the 15,16-bond fission by leading to the mesomeric immonium system in (XI), longer by one double bond than the corresponding system produced from 19,20-dihydroakuammicine. That the latter compound decomposes at all is an indication that pyridinium ion formation is not essential for the 15,16-bond fission.

Concerning the decomposition of akuammicine at 140°, we have observed that the betaine (I), its hydrochloride (XII; R = H, X = Cl), and the methyl ester of the picrate (XII; R = Me, X = picrate) survive largely undecomposed in methanol at 140° for 3 hr. No carbazole formation was observed. Treatment of the betaine (I), and the methyl ester of the chloride (XII; R = Me, X = Cl), with an excess of sodium methoxide and magnesium methoxide in methanol at 140° for 3 hr. results in decomposition, with the isolation of 3-ethylpyridine from the methanol distillates. Ultraviolet spectroscopic examination of the residues showed in the first case only indole absorption, and, in the second, that only a trace of 2-hydroxycarbazole accompanied the mainly indole product.

The results suggest that the elimination of 3-ethylpyridine from the methyl ester (XII; R = Me, X = OMe) in the actual decomposition of akuammicine in methanol at 140° is brought about by the methoxide ion, and is thus a Hofmann reaction. These results also show that in the presence of a large excess of methoxide ions the simple cyclisation of the vinylindole (II) to 2-hydroxycarbazole is replaced by conversion into an indole, the nature of which has not been investigated.

XUM

Experimental

Decomposition of Akuammicine in Methanol at 140°.—A solution of akuammicine (400 mg.) in dry methanol (6 c.c.) was heated in an evacuated sealed tube at 140° for 2 hr. The methanol was distilled from the dark solution, more methanol (10 c.c.) added to the residue, and the solution evaporated again. This process was repeated eight times. The combined distillates were acidified with concentrated hydrochloric acid (0·2 c.c.) and evaporated. The residue was crystalline and deliquescent (85 mg., 48%); treatment with aqueous sodium picrate gave 3-ethylpyridine picrate which, after crystallisation from aqueous methanol, had m. p. and mixed m. p. 124·5—126·5° (Found: C, 46·75; H, 3·75. Calc. for $C_{13}H_{12}N_4O_7$: C, 46·4; H, 3·6%). The non-volatile portion of the reaction mixture (251 mg.) was chromatographed on neutral alumina (10 g.): none of the fractions had an akuammicine-type chromophore, and the 9 : 1 chloroform–methanol fraction yielded the crude 2-hydroxycarbazole (135 mg., 60%). Sublimation at 160°/0·05 mm. followed by crystallisation from benzene–methanol gave pure 2-hydroxycarbazole, m. p. 270—273° (sealed capillary), undepressed by admixture with an authentic specimen [3] (Found: C, 78·6; H, 5·0; N, 7·75; OMe, 0·0. Calc. for $C_{12}H_9NO$: C, 78·7; H, 4·95; N, 7·65; OMe, 0·0%), $\lambda_{max.}$ 235, 258, 301 mμ in EtOH (ε 54,000, 25,000, 15,500 respectively), changed to 243, 330 mμ (ε 48,000, 20,000 respectively) by alkali, $\nu_{max.}$ (in Nujol) 3400 (NH str.), 3220 cm.$^{-1}$ broad (OH str.; hydrogen-bonded). The ultraviolet spectra in neutral and alkaline solution were identical with those of authentic 2-hydroxycarbazole. The picrate forms dark red needles (from benzene), m. p. 182—186° (decomp.). The *O*-acetyl derivative, prepared by the pyridine–acetic anhydride method, forms plates (from methanol), m. p. 185—187°, undepressed by admixture with 2-acetoxycarbazole,[4] $\lambda_{max.}$ 233, 257, 295, 320, 332 mμ in EtOH (ε 39,000, 17,500, 14,800, 4000, 2950 respectively), $\nu_{max.}$ (in Nujol) 3420 (NH str.), 1755 cm.$^{-1}$ (C=O str.).

Decomposition of Akuammicine in Methanol at 80°.—A solution of akuammicine (470 mg.) in dry methanol (10 c.c.) was heated in an evacuated sealed tube at 80° for 3 hr. The orange-red solution was evaporated to a small volume, then benzene (15 c.c.) was added, and the remaining methanol removed completely by evaporation to dryness. The benzene-soluble portion of the residue was chromatographed on neutral alumina. The 49 : 1 ether–methanol fraction (316 mg.) had m. p. 170—179·5°, $[\alpha]_D^{21}$ −680° (*c* 0·19 in MeOH), and an ultraviolet spectrum identical with that of akuammicine–ψ-akuammicine, but with ε values about 5·5% low. If we assume a non-rotating contamination the rotation on the basis of the intensity of the akuammicine–ψ-akuammicine 330 mμ band in this material is $[\alpha]_D^{21}$ −728°, which is of the order of that of pure akuammicine.

The benzene-insoluble fraction of the decomposition (127 mg.) [$\nu_{max.}$ (in Nujol) 3600—2100s, 1735m; sh,1650m, 1600s cm.$^{-1}$] was dissolved in methanol, and the solution evaporated to dryness *in vacuo*, to yield a foam which was thoroughly digested with water (4 c.c.). Evaporation of the filtered aqueous extract gave 1-[2-(2-*carboxymethyl*-3-*indolyl*)*ethyl*]-3-*ethylpyridinium betaine* as a yellow glass (87 mg.) which crystallised from methanol–acetone as small pale yellow needles with variable decomposition point (between 150° and 180°) (Found, in material dried at room temperature: C, 69·2; H, 6·7. $C_{19}H_{20}N_2O_2,H_2O$ requires C, 69·9; H, 6·8. Found, in material dried at 100° *in vacuo*: C, 73·4; H, 6·75. $C_{19}H_{20}N_2O_2$ requires C, 74·0; H, 6·55%), $\lambda_{max.}$ 223, 268, 290 mμ in MeOH (ε 31,600, 9550, 6300 respectively), $\lambda_{infl.}$ 280 mμ (ε 7600). An equimolar mixture of 2,3-dimethylindole and 3-methylpyridine ethobromide had $\lambda_{max.}$ 225, 268, 273, 290 mμ (ε 33,000, 9800, 9800, 6300 respectively), $\lambda_{infl.}$ 280 mμ (ε 7600).

The betaine formed a *picrate* crystallising from methanol as yellow prisms, m. p. 153—154° (decomp.) (Found, in material dried at room temperature *in vacuo*: C, 55·6; H, 4·4; N, 12·3; OMe, 0·95. $C_{19}H_{20}N_2O_2,C_6H_3N_3O_7,0{\cdot}25CH_3{\cdot}OH$ requires C, 55·6; H, 4·45; N, 12·8; OMe, 1·4. Found, in material dried at 100° *in vacuo*: C, 55·7; H, 4·3; N, 12·85; OMe, 0·65. $C_{19}H_{20}N_2O_2,C_6H_3N_3O_7$ requires C, 55·8; H, 4·3; N, 13·0; OMe, 0·0%), $\nu_{max.}$ (in Nujol) 3400m (NH str.), 3300—2300vw (diffuse; OH stretch), 1703s cm.$^{-1}$ (C=O str.).

Decomposition of Akuammicine in Methanol at 100°.—A solution of akuammicine (330 mg.) in commercial methanol (10 c.c.) was heated in an evacuated sealed tube at 100° for 3 hr. The benzene-insoluble material (263 mg., 80%), when worked up as for the decomposition at 80°,

[3] Joule and Smith, *Proc. Chem. Soc.*, 1959, 322; Smith and Wróbel, *J.*, 1960, 792.
[4] Cummins and Tomlinson, *J.*, 1955, 3475.
[4] I.G. Farbenind, A.-G., Fr. 666,450, Dec. 1928; *Chem. Abs.*, 1930, **24**, 1391.

yielded the betaine (I) (238 mg.) which with methanolic picric acid formed yellow prisms (405 mg., 70%), m. p. 153—154° (decomp.).

Epimerisation of 2,16-*Dihydroakuammicine in Methanol at* 100°.—2,16-Dihydroakuammicine (36 mg.) in dry methanol (1 c.c.) was heated in an evacuated sealed tube at 100° for 12 hr. The product was chromatographed on neutral alumina with ether as the eluant, to give crude starting material, m. p. 125—138° (6 mg.), and the epimerised ester (28 mg.). This product was crystallised twice from methanol–water and once from light petroleum, to give pure *methyl* 2β,16α-*cur*-20-*en*-17-*oate* as needles, m. p. 156·5—158° (Found: C, 73·85; H, 7·55. $C_{20}H_{24}N_2O_2$ requires C, 74·05; H, 7·45%).

The above product (4·5 mg.) was hydrogenated in 2 : 1 methanol–acetic acid (3 c.c.) in the presence of Adams catalyst (2 mg.). After 4 hr., the product was worked up, and crystallised from methanol, and then from light petroleum, to give needles, m. p. 148—152°, undepressed by authentic methyl 2β,16α,20α-curan-17-oate.[1]

19,20-*Dihydroakuammicine in Methanol at* 100°.—19,20-Dihydroakuammicine (5·6 mg.) in dry methanol (0·3 c.c.) was heated in an evacuated sealed tube at 100° for 5 hr. The product was extracted with light petroleum: the petroleum extract (5 mg.) crystallised from light petroleum to give needles, m. p. 155—163·5°, undepressed on admixture with the starting material, m. p. 166—167·5°. The petroleum insoluble residue (0·5 mg.) showed an indole-type ultraviolet spectrum.

19,20-*Dihydroakuammicine in Methanol at* 140°.—A solution of 19,20-dihydroakuammicine (41 mg.) in dry methanol (1 c.c.) was heated in an evacuated sealed tube at 140° for 3 hr. The yellow solution was worked up as for the decomposition of akuammicine at 140°. Crude starting material (8 mg.) and 2-hydroxycarbazole (2·4 mg.) were isolated by chromatography of the non-volatile portion; 3-ethylpyridine picrate (4 mg.), m. p. 110—120°, raised to m. p. 115—124° on admixture with an authentic specimen, was isolated from the methanol distillate.

Esterification of the Betaine Picrate.—A solution of the betaine picrate (53 mg.) in 1 : 1 acetone–methanol (3 c.c.) was treated with an excess of diazomethane in ether (3 c.c.), then the dark red solution was evaporated to small volume (1 c.c.) and treated with charcoal and picric acid (5 mg.). The filtered solution deposited orange prisms (45 mg.), m. p. 168—171°. A further crystallisation from acetone–methanol (charcoal) gave the pure *ester picrate* as yellow prisms, m. p. 170—172° (Found, in material dried at 100° *in vacuo*: C, 57·1; H, 4·6; N, 12·4; OMe, 5·6. $C_{26}H_{25}O_9N_5$ requires C, 56·6; H, 4·6; N, 12·7; OMe, 5·6%), $\nu_{max.}$ (in Nujol) 3280m (NH str.), 1744s cm.$^{-1}$ (C=O str.).

Action of Methanolic Methoxide on the Betaine (I).—A solution of the betaine (I) (10 mg.) in methanol (1 c.c.) in which sodium (5 mg.) and magnesium (5 mg.) had been dissolved was heated in an evacuated sealed tube at 140° for 3 hr. The methanol was distilled, then more methanol (3 c.c.) added to the residue, and the solution evaporated again. This process was repeated three times. The combined distillates were acidified with concentrated hydrochloric acid (1 drop) and evaporated; treatment with aqueous sodium picrate gave 3-ethylpyridine picrate (3 mg.), m. p. and mixed m. p. 124—126·5°. The residue showed an indole-type ultraviolet spectrum.

Action of Methanolic Methoxide on the Ester Chloride (XII; R = Me, X = Cl).—A solution of the betaine (8·0 mg.) in methanol (0·1 c.c.) was treated with concentrated hydrochloric acid (1 drop), then the solvent and excess of acid were removed *in vacuo*. The residue was dissolved in methanol (0·5 c.c.) and treated with excess of diazomethane in ether (0·5 c.c.), then evaporated to dryness *in vacuo*. Methanol (1 c.c.), in which sodium (5 mg.) and magnesium (5 mg.) had been dissolved, was added to the residue, and the solution heated in an evacuated sealed tube at 140° for 3 hr. The solution was worked up as described for the action of methoxide on the betaine, to give 3-ethylpyridine picrate (2 mg.), m. p. and mixed m. p. 120—126°. The non-volatile residue was partitioned between saturated sodium hydrogen carbonate (5 c.c.) and chloroform (2 c.c.), then the aqueous phase was re-extracted with chloroform (2 × 2 c.c.) and the combined chloroform extracts were chromatographed on neutral alumina. The 9 : 1 chloroform–methanol fraction (2 mg.) showed an ultraviolet spectrum in methanol with a nearly flat peak from 260 to 300 mμ, which on the addition of alkali developed a peak at 325 mμ.

We are indebted to Dr. M. Tomlinson for a specimen of 2-hydroxycarbazole and to the D.S.I.R. for a maintenance grant (to P. N. E.).

THE UNIVERSITY, MANCHESTER, 13. [*Received, August 26th,* 1960.]

XUM

288. *Derivatives of 3-Acetamido-3-deoxy-D-altrose and Their Conversion into 2-Acetamido-2-deoxy-D-ribose.**

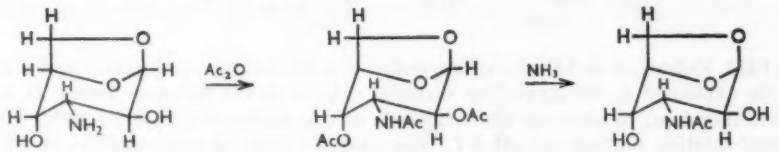
By Bruce Coxon and L. Hough.

3-Acetamido-3-deoxy-D-altrose has been prepared from 3-amino-1,6-anhydro-3-deoxy-β-D-altropyranose, and its periodate oxidation investigated. This hexose derivative was not oxidized to any large extent in the pyranose form.

Oxidation of the diethyl dithioacetal of 3-acetamido-3-deoxy-D-altrose with peroxypropionic acid gave a mixture of (2-acetamido-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane and 2-acetamido-2-deoxy-D-ribose.

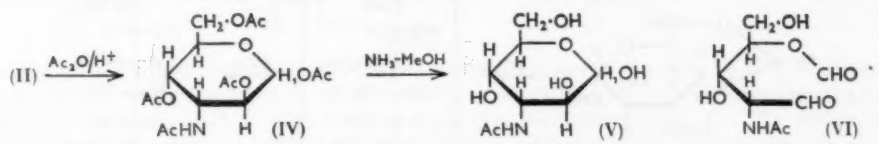
Current biochemical interest in amino-sugars prompted an investigation of the synthesis of 2-acetamido-2-deoxy-D-ribose (XV) by removal of $C_{(1)}$ from derivatives of 3-acetamido-3-deoxy-D-altrose which are readily synthesized from D-glucose.

Hydrolysis of methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside [1,2] with hydrochloric acid gave the hydrochloride of 3-amino-1,6-anhydro-3-deoxy-β-D-altropyranose (I) which was presumably formed through 3-amino-3-deoxy-D-altrose. This



(I) (II) (III)

anhydro-compound (previously named "anhydroepiglucosamine" [3]) was presumed [2] to be a 1,6-anhydro-derivative by analogy with 1,6-anhydro-β-D-altropyranose. Acetylation gave 3-acetamido-2,4-di-*O*-acetyl-1,6-anhydro-3-deoxy-β-D-altropyranose (II) which, on de-*O*-acetylation in methanolic ammonia, yielded 3-acetamido-1,6-anhydro-3-deoxy-β-D-altropyranose (III). In agreement with the 1,6-anhydro-structure, the last derivative did not consume periodate, whereas the parent 3-amino-3-deoxy-derivative (I) consumed



two mol. of periodate and gave one mol. of titratable acid. Similar results were obtained for 2-amino-1,6-anhydro-2-deoxy-β-D-altropyranose by Foster, Stacey, and Vardheim.[4] The triacetyl derivative (II) was remarkably soluble in water as a result of the hydrophilic nature of the acetamido-group, which apparently counteracts the hydrophobic properties of the acetoxy-group. Fischer and Richardson [5] tell us that 3-acetamido-2,4-di-*O*-acetyl-1,6-anhydro-3-deoxy-β-D-gulopyranose is also soluble in water.

Acetolysis [6] of the triacetyl derivative (II) with sulphuric or perchloric acid [7] as catalyst

* For a preliminary account of this work see Coxon and Hough, *Chem. and Ind.*, 1959, 1249.

[1] Robertson, Myers, and Tetlow, *Nature*, 1938, **142**, 1076; Myers and Robertson, *J. Amer. Chem. Soc.*, 1943, **65**, 8; Baker and Schaub, *J. Org. Chem.*, 1954, 646.

[2] Wiggins, *J.*, 1947, 18.

[3] Levene and Meyer, *J. Biol. Chem.*, 1923, **55**, 221.

[4] Foster, Stacey, and Vardheim, *Acta Chem. Scand.*, 1958, **12**, 1605.

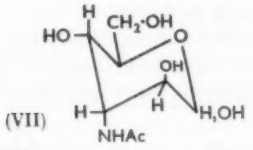
[5] Fischer and Richardson, personal communication.

[6] Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1727.

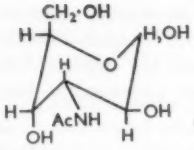
[7] Bredereck, Wagner, Hagelloch, and Faber, *Chem. Ber.*, 1958, **91**, 515; Richtmyer and Pratt, *J. Amer. Chem. Soc.*, 1956, **78**, 4717.

gave 3-acetamido-1,2,4,6-tetra-*O*-acetyl-3-deoxy-αβ-D-altropyranoses (IV). Methanolic ammonia rather slowly (*ca.* 24 hr.) deacetylated this to 3-acetamido-3-deoxy-D-altrose (V) which crystallized after paper chromatography or fractional elution from charcoal.[8]

Periodate oxidation of 3-acetamido-3-deoxy-D-altrose was examined at pH 3·7,[9] since reaction in the pyranose form (V) with 1 mol. of periodate would have given 2-acetamido-2-deoxy-4-*O*-formyl-D-ribose (VI). Formyl esters of this type are usually[9] stable to periodate under these conditions of pH. However, a mutarotated solution of 3-acetamido-3-deoxy-D-altrose (V) at pH 3·7 reacted quickly (1 hr.) with two mol. of periodate and then slowly (24 hr.) with a further mol.; 0·7 mol. of formaldehyde was rapidly (2 min.) released. These results are consistent with the oxidation of the majority of 3-acetamido-3-deoxy-D-altrose in the furanose or acyclic form, rather than the pyranose form (V), both conformations of which (VII and VIII) are unstable because of axial interactions (see Reeves[10] and Barker and Shaw[11]).



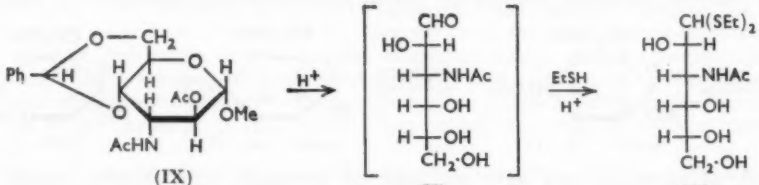
(VII)



(VIII)

In 1943, Richtmyer and Hudson[12] suggested that the complex mutarotation of D-altrose could be explained if the crystalline material existed in the furanose form. It was of interest, therefore, to examine the oxidation of crystalline D-altrose by sodium metaperiodate solution buffered to pH 3·7; this gave 0·4 mol. of formaldehyde in 2·5 min. These results show that only 30% of 3-acetamido-3-deoxy-D-altrose and 60% of D-altrose are oxidized in the pyranose form, and that furanose and/or acyclic forms play a significant part.

McEvoy, Baker, and Weiss[13] found it possible to remove $C_{(1)}$ from 3-acetamido-3-deoxy-6-*O*-triphenylmethyl-D-altrose by oxidative cleavage with lead tetra-acetate, but with periodate the reaction was unsuccessful. They commented that the pyranose



(IX) (X) (XI)

configuration of the triphenylmethyl derivative had been assumed without evidence and hence this product was, or contained quantities of, the corresponding altrofuranose.

In direct contrast, 2-acetamido-2-deoxy-D-arabinose was prepared by the periodate cleavage of 3-acetamido-3-deoxy-D-mannopyranose,[14] presumably because the C1 chair conformation of 3-acetamido-3-deoxy-D-mannopyranose is more stable than that of the D-*altro*-isomer.

Attention was then turned to the disulphone method of shortening the carbon chain of

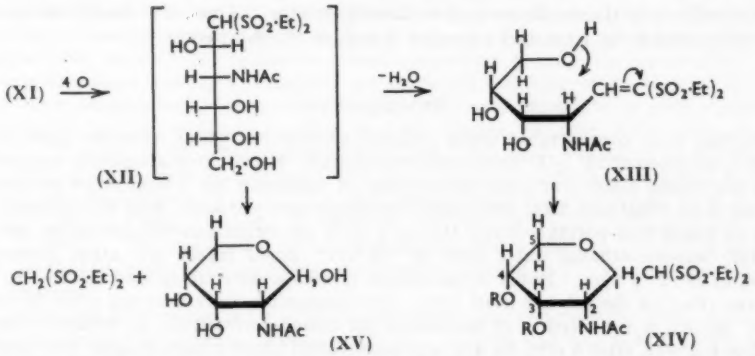
[8] Andrews, Hough, and Powell, *Chem. and Ind.*, 1956, 658.
[9] Hough, Taylor, Thomas, and Woods, *J.*, 1958, 1212.
[10] Reeves, *Adv. Carbohydrate Chem.*, 1951, **6**, 107.
[11] Barker and Shaw, *J.*, 1959, 584.
[12] Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 740.
[13] McEvoy, Baker, and Weiss, *J. Amer. Chem. Soc.*, 1960, **82**, 209.
[14] Baer and Fischer, *J. Amer. Chem. Soc.*, 1960, **82**, 3709.

aldoses.[15,16] Treatment of 3-acetamido-3-deoxy-D-altrose at 0° with ethanethiol and concentrated hydrochloric acid [17] gave a complex mixture, as revealed by paper chromatography, from which 3-acetamido-3-deoxy-D-altrose diethyl dithioacetal (XI) crystallized.

A more convenient preparation with an improved yield (23%) of the dithioacetal (XI) from methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside was acetylation to give the methyl 3-acetamido-2-*O*-acetyl derivative [18] (IX) followed by treatment with concentrated hydrochloric acid and ethanethiol at room temperature. The latter reaction caused the removal of the benzylidene, glycosidic methoxyl, and 2-*O*-acetyl groups with simultaneous thioacetal formation from the resultant 3-acetamido-3-deoxy-D-altrose (X).

Oxidation of the dithioacetal (XI) with peroxypropionic acid in methanol at −10° was expected to give the diethylsulphonylpyranosylmethane derivative (XIV; R = H) by the formation of the hexenetriol (XIII) from the hexanetetraol (XII) followed by cyclization. (The dithioacetals of D-glucose, D-mannose, and D-galactose gave diethylsulphonylpyranosylmethanes by this process.[15]) However, paper chromatography of the product revealed another compound which, after separation, was shown to be 2-acetamido-2-deoxy-D-ribose (XV). This pentose was identical with that prepared similarly from 3-acetamido-3-deoxy-D-allose diethyl dithioacetal,[19] and undoubtedly arose by cleavage of the 1,2-bond in the unstable tetraol intermediate (XII).

The pyranose structure of the disulphone was supported by its behaviour in pyridine,



where no red colour developed, a reaction which is typical of the hex-1-ene derivatives (*e.g.*, XIII); and no cleavage to the acetamidopentose (XV) and diethylsulphonylmethane was observed, as would be expected [15] of the acyclic hexanetetraol (XII). The isolation of a crystalline triacetate (XIV; R = Ac) which was identical with that prepared in the same way [19] from 3-acetamido-3-deoxy-D-allose derivatives, confirmed the cyclic structure.

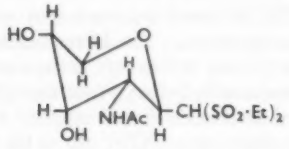
Conformational analysis was then used to predict the configuration at $C_{(1)}$, as in the case of other diethylsulphonylpyranosylmethanes.[15]

Two chair conformations of 1-(2-acetamido-2-deoxy-D-ribopyranosyl)diethylsulphonylmethane (XIV; R = H) are possible in which the large, polar diethylsulphonylmethyl group is in an equatorial position. The 1C chair conformation (XVII) with the diethylsulphonylmethyl group in the α-configuration has a 2,4-diaxial interaction involving the large acetamido-group and a hydroxyl group. On the other hand, the C1 conformation (XVI) has only one axial substituent, namely, a 3-hydroxyl group, and hence this conformation, with the diethylsulphonylmethyl group in the β-configuration, is to be preferred.

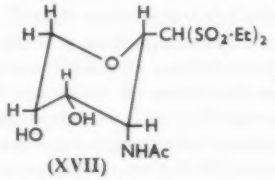
[15] Hough and Taylor, *J.*, 1956, 970.
[16] Barker and MacDonald, *J. Amer. Chem. Soc.*, 1960, **82**, 2297; MacDonald and Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 2087; *Biochim. Biophys. Acta*, 1953, **12**, 203.
[17] Hough and Taha, *J.*, 1956, 2042.
[18] Robertson and Myers, *Nature*, 1939, **143**, 640.
[19] Coxon and Hough, *Chem. and Ind.*, 1959, 1249.

XUM

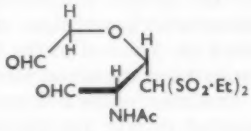
Since the glycosides of 2-acetamido-2-deoxy-D-ribose were not available, it was not possible to apply Hudson's isorotation rules directly [15] to the cyclic disulphone (XIV; R = H; $[M]_D$ −11,690°). The molecular rotations of methyl α-D-ribopyranoside [20] ($[M]_D$ +16,920°) and methyl β-D-ribopyranoside [21] ($[M]_D$ −17,260°) were therefore used as



(XVI)



(XVII)



(XVIII)

a basis for comparison. The value of *B* (−170°) gave a negative value for *A* (−11,520°), providing further support for the β-configuration of the diethylsulphonylmethyl group, and the cyclic disulphone is, therefore, termed (2-acetamido-2-deoxy-β-D-ribopyranosyl)-diethylsulphonylmethane (XVI).

As with other diethylsulphonylpyranosylmethanes,[15] (2-acetamido-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane reacted with more periodate than is required for glycol cleavage because of breakdown of the dialdehyde (XVIII) due to the combined inductive effects of the sulphone and acetamido-groups. Thus, the disulphone consumed 2 mol. of periodate in 1 hr. and a further 2 mol. in the next 60 hr.

Experimental

Solutions were concentrated under reduced pressure. Optical rotations were measured for $CHCl_3$ solutions at 24° ± 1° unless otherwise stated. Paper chromatography was performed by the descending method at room temperature on Whatman No. 1 filter paper for qualitative purposes or on Whatman 3MM filter paper for preparative purposes, with the following mobile phases (i) butan-1-ol–pyridine–water (10 : 3 : 3 v/v), (ii) butan-1-ol–ethanol–water (40 : 11 : 19 v/v), (iii) benzene–ethanol–water (169 : 47 : 15 v/v; upper layer), (iv) ethyl acetate–acetic acid–water (9 : 2 : 2 v/v). Rates of movement of compounds are quoted relative to that of rhamnose (R_{Rh}) or the solvent front (R_F). The compounds were detected with the following sprays; (*a*) 1% w/v ninhydrin in butan-1-ol (for amino-derivatives), (*b*) 0·02M-sodium metaperiodate followed after 5 min. by 4% w/v ammoniacal silver nitrate reagent (for diols, triols, etc.), (*c*) 4% w/v ammoniacal silver nitrate (for reducing sugars and dithioacetals), (*d*) *p*-anisidine hydrochloride in butan-1-ol–ethanol–water (for reducing sugars), and (*e*) Elson–Morgan reagents [22] (for 2-acetamido-sugars). M. p.s were determined on a Kofler microheating stage. Infrared absorption spectra were determined in Nujol mulls with a Unicam S.P. 100 spectrometer. Decolorizations were carried out in alcoholic solutions by B.D.H. acid-washed charcoal, further washed before use with water followed by alcohol.

3-*Amino*-1,6-*anhydro*-3-*deoxy*-β-D-*altropyranose* (I) *Hydrochloride*.—Methyl 3-amino-4,6,-*O*-benzylidene-3-deoxy-α-D-altropyranoside [1,2] (5 g.) in 1% w/v hydrochloric acid (200 ml.) was heated at 100° for 22 hr. The cooled solution was washed with chloroform to remove benzaldehyde, decolorized, and concentrated to a syrup which crystallized when kept over sodium hydroxide. Recrystallization from methanol yielded the hydrochloride as cubes (1·2 g., 35%), m. p. 205—215° (decomp.), $[\alpha]_D^{21}$ −175° (*c* 0·51 in H_2O), R_{Rh} 0·36 (solvent i; brown spot with spray *a*) (Found: C, 36·6; H, 6·1; N, 7·0. Calc. for $C_6H_{12}ClNO_4$: C, 36·4; H, 6·1; N, 7·1%). Levene and Meyer [3] record m. p. 216° (decomp.), $[\alpha]_D^{20}$ −172° (*c* 1 in 2·5% HCl).

3-*Acetamido*-2,4-*di*-O-*acetyl*-1,6-*anhydro*-3-*deoxy*-β-D-*altropyranose* (II).—Methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside (64 g.) was hydrolysed in 4% w/v hydrochloric acid (720 ml.) at 100° for 48 hr. The cooled solution was then extracted with chloroform

[20] Barker and Smith, *J.*, 1954, 2151.
[21] Jackson and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1229.
[22] Kent and Whitehouse, "Biochemistry of the Amino-sugars," Butterworths, London, 1955, p. 164, and references therein.

(2 × 50 ml.) to remove benzaldehyde, concentrated to *ca.* one-third of the initial volume, and decolorized. Further concentration gave a pale green syrup of (mainly) 3-amino-1,6-anhydro-3-deoxy-β-D-altropyranose hydrochloride. The syrupy amino-derivative was treated with dry pyridine (270 ml.) and acetic anhydride (250 ml.) at 28° for 45 hr., and the solution was concentrated to remove pyridine and acid anhydride. The dark red solution was then poured on ice and sodium hydrogen carbonate, and the suspension was continuously extracted with chloroform for 3 hr. Evaporation of the extract afforded a brown syrup which was decolorized, and crystallized from ethanol, giving needles of the *triacetyl derivative* (41 g., 63% overall), m. p. 176—177° unchanged after a further recrystallization from ethanol. The derivative was soluble in water and had $[\alpha]_D$ −147° (*c* 0·44 in H_2O) (Found: C, 50·2; H, 6·3; N, 4·9; Ac, 41·3, 39·6. $C_{12}H_{17}NO_7$ requires C, 50·2; H, 6·0; N, 4·9; Ac, 45·0%), $\nu_{max.}$ 3300m and 1562s (NH), 1752s and 1738s (*O*-Ac), 1655s (*N*-Ac) cm.$^{-1}$.

3-Acetamido-1,6-anhydro-3-deoxy-β-D-altropyranose (III).—3-Acetamido-2,4-di-*O*-acetyl-1,6-anhydro-3-deoxy-β-D-altropyranose (1·01 g.) in methanol (25 ml.) was treated with liquid ammonia until the solution was saturated, and kept at room temperature for 3·5 hr. Concentration then gave a syrup, from which acetamide was removed by sublimation at 100°/15 mm. When seeded and triturated with methanol–acetone, the syrup crystallized, yielding the *N-acetyl derivative* (0·57 g., 80%), m. p. 159—160°, $[\alpha]_D$ −235° (*c* 1·14 in H_2O) (Found: C, 47·3; H, 6·6; N, 6·5; Ac, 22·5. $C_8H_{13}O_5N$ requires C, 47·3; H, 6·5; N, 6·9; Ac, 21·2%); this did not consume periodate during 48 hr.

3-Acetamido-1,2,4,6-tetra-O-acetyl-3-deoxy-αβ-altropyranoses (IV).—3-Acetamido-2,4-di-*O*-acetyl-1,6-anhydro-3-deoxy-β-D-altropyranose {1·06 g.; $[\alpha]_D$ −195° (*c* 4·24 in acetic anhydride)} was dissolved in acetic anhydride (50 ml.) containing concentrated sulphuric acid (1 ml.). After 0·5 hr. at room temperature the solution had $[\alpha]_D$ +44·2° (calc. as penta-acetyl derivative). unchanged after 18 hr. The colourless mixture was then poured into an ice-cold aqueous suspension of sodium hydrogen carbonate and extracted with chloroform (5 × 30 ml.). The extracts were washed with water, dried ($CaSO_4$), and concentrated to a syrupy mixture of penta-acetates (1·17 g., 81%), $[\alpha]_D$ +27·0° (*c* 4·66) (Found: Ac, 48. Calc. for $C_{16}H_{23}O_{10}N$: Ac, 55%). The use of 60% aqueous perchloric acid [7] (1·1 equiv.) in place of sulphuric acid gave a syrup of similar specific rotation. One preparation crystallized in part from methanol–ether to give a *penta-acetate* (0·16 g., 41%) that, recrystallized from methanol–ether, had m. p. 161°, $[\alpha]_D$ +4·0° (*c* 1·38%) (Found: C, 49·0; H, 6·2; N, 3·8. $C_{16}H_{23}NO_{10}$ requires C, 49·3; H, 6·0; N, 3·6%). The preparation of the crystalline derivative was not, however, reproducible, but on de-*O*-acetylation with ammonia the crystals yielded 3-acetamido-3-deoxy-D-altrose as did the syrup.

3-Acetamido-3-deoxy-D-altrose (V).—The syrupy penta-acetyl derivative (1·5 g.) in methanol (30 ml.) was added to aqueous ammonia (30 ml.; *d* 0·88) and the mixture kept at room temperature for 24 hr. Concentration of the solution then gave a pale yellow syrup of *3-acetamido-3-deoxy-D-altrose*, R_{Rh} 0·80 [solvent i; sprays *b*, *c*, and *d* (yellow spot)]. The product was purified by chromatography on large sheets of Whatman 3MM paper, or by adsorption on a squat column of B.D.H. acid-washed charcoal [8] followed by elution with water. Crystallization of the reducing sugar was difficult, but occurred when a methanolic solution evaporated slowly at 0° during 2—3 months. The powder obtained, m. p. 143—146 (decomp.), recrystallized from methanol, then having m. p. 151—153° (decomp.), $[\alpha]_D$ −35° (constant; 24 hr.; *c* 1·28 in H_2O) (Found: C, 43·5; H, 7·1; N, 5·8. $C_8H_{15}NO_6$ requires C, 43·5; H, 6·9; N, 6·3%), $\nu_{max.}$ 3290s 3190s, (OH and NH), 1620s (*N*-Ac), 1568s (NH). De-*O*-acetylation with sodium methoxide in methanol followed by de-ionization with Amberlite IR-120 (H^+) resin, gave a lower yield owing to hydrolysis of the *N*-acetyl group. When 3-acetamido-3-deoxy-D-altrose was used for later preparations, it was more convenient to use the syrup obtained initially from the penta-acetyl derivative.

Methyl 3-Acetamido-2-O-acetyl-4,6-O-benzylidene-3-deoxy-α-D-altropyranoside (IX).—Methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside in pyridine–acetic anhydride yielded, by the usual procedure, the diacetyl derivative as plates, m. p. 199—200°, $[\alpha]_D^{22}$ +17° (*c* 1·47). Robertson and Myers [18] recorded m. p. 201°, $[\alpha]_D$ +14·6°.

3-Acetamido-3-deoxy-D-altrose Diethyl Dithioacetal (XI).—(*a*) 3-Acetamido-3-deoxy-D-altrose (0·35 g.) in ethanethiol (2 ml.) and concentrated hydrochloric acid (2·4 ml.; *d* 1·18) was shaken at 0° for 28 hr. The emulsion was then diluted with methanol (30 ml.) and neutralized with lead carbonate, and insoluble residues were filtered off and washed with hot methanol (30 ml.).

Concentration of the combined filtrate and washings gave a pale yellow syrup (0·37 g.) which was decolorized. Paper chromatography revealed a mixture of at least five components which had R_P 0·07, 0·17 (solvent i; sprays *a* and *b*), 0·45, 0·73, 0·82 (solvent i; spray *b*). The component with R_P 0·73 crystallized from methanol–ether, yielding 3-*acetamido*-3-*deoxy*-D-*altrose diethyl dithioacetal* (0·127 g., 25%), m. p. 135—138°, that, recrystallized from methanol–ether and washed with methanol, had m. p. 146—147°, $[\alpha]_D$ +26·2° (*c* 1·05 in MeOH) (Found: C, 44·0; H, 7·7; N, 4·3; S, 19·3; Ac, 14·0. $C_{12}H_{25}NO_5S_2$ requires C, 44·0; H, 7·7; N, 4·3; S, 19·6; Ac, 13·2%).

(*b*) Methyl 3-acetamido-2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside (0·43 g.) was shaken with ethanethiol (2 ml.) and concentrated hydrochloric acid (2 ml.; *d* 1·18) at room temperature for 6·5 hr. The mixture was then diluted with methanol (30 ml.) and neutralized with lead carbonate, and the insoluble residues were filtered off and washed in hot methanol. Concentration of the combined filtrate and washings yielded an emulsion which was treated with acetic anhydride (3 ml.) overnight, in order to complete *N*-acetylation. The anhydride was then distilled off and a syrup obtained which was decolorized; crystallized from ethanol–ether it yielded 3-acetamido-3-deoxy-D-altrose diethyl dithioacetal (0·09 g., 23%), m. p. 144—145°, undepressed on admixture with the previous preparation. Paper chromatography of the mother-liquors revealed the same mixture as was obtained before, except for a faint spot near the solvent front (benzaldehyde diethyl dithioacetal ?).

When the above reaction was repeated at 0° for 22 hr., the 3-acetamido-3-deoxy-D-altrose dithioacetal was isolated in lower yield (8%). Acetylation of the dithioacetal in pyridine–acetic anhydride afforded the *tetra*-O-*acetate* which crystallized as rods, m. p. 110° (Found: C, 48·1; H, 6·6. $C_{20}H_{33}NO_9S_2$ requires C, 48·4; H, 6·7%).

Oxidation of 3-*Acetamido*-3-*deoxy*-D-*altrose Diethyl Dithioacetal by Peroxypropionic Acid.*—The diethyl dithioacetal (0·21 g.) in methanol (25 ml.) was cooled to −10°, and aqueous peroxypropionic acid [23] (5 ml.) added in small portions with shaking. The mixture was kept at −10° for 2·5 hr. and then concentrated to a colourless hygroscopic syrup from which traces of peroxypropionic acid were removed by repeated dissolution in methanol and reconcentration (yield 0·25 g.). Paper chromatography of the syrup, with spray *b*, showed the presence of two components with R_{Rh} 1·1 and 1·5 (solvent iv), and R_{Rh} 1·0 and 1·6 (solvent i). The two components of the syrup were separated by paper chromatography with solvent ii for 14 hr. The separated compounds were then detected with spray *b* and eluted from the appropriate zones with warm methanol. The slower moving component (R_{Rh} 1·1) was obtained as a syrup (0·048 g.) which crystallized from methanol–ether, to give 2-*acetamido*-2-*deoxy*-D-*ribose* (XV) (0·018 g.), m. p. 136—139°, R_P 0·44 [solvent i; sprays *b*, *d* (orange spot), *c*, and *e* (violet spot)] (Found: C, 43·4; H, 6·8. $C_7H_{13}NO_5$ requires C, 44·0; H, 6·9%), $\nu_{max.}$ 3440s and 3350s (OH and NH), 1565s (NH), 1600s (*N*-Ac).

The faster-moving zone of the chromatogram (R_{Rh} 1·5) yielded (2-*acetamido*-2-*deoxy*-β-D-*ribopyranosyl*)*diethylsulphonylmethane* (XVI), a syrup (0·087 g.), $[\alpha]_D^{26}$ −31·3° (*c* 5·66 in MeOH) (Found: C, 38·8; H, 6·4; N, 3·8; S, 18·1; Ac, 13·9. $C_{13}H_{23}NO_8S_2$ requires C, 38·6; H, 6·2; N, 3·8; S, 17·2; Ac, 11·5%). The syrup did not give a red colour with dry pyridine, suggesting that unsaturated disulphones were absent.

(2-*Acetamido*-3,4-*di*-O-*acetyl*-2-*deoxy*-β-D-*ribopyranosyl*)*diethylsulphonylmethane* (XIV; R = Ac).—(2-Acetamido-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane (0·08 g.) was dissolved in acetic anhydride (5 ml.), concentrated sulphuric acid (1 drop) added, and the mixture heated at 95—100° for 1 hr. The dark solution was then cooled to room temperature, poured into ice and sodium hydrogen carbonate, and extracted with chloroform (5 × 15 ml.). The combined extracts were washed with water, dried ($CaSO_4$), and concentrated to a pale yellow syrup which was decolorized (yield 0·094 g., 96%). Crystallization from acetone–light petroleum (b. p. 60—80°) afforded needles (0·035 g., 35%), m. p. 181—183°; recrystallized from the same solvents and washed with a little ethereal acetone, the *triacetyl derivative* had m. p. 183—185°, $[\alpha]_D$ −16·8° (*c* 1·34) (Found: C, 42·2; H, 6·0; N, 3·1; S, 13·1. $C_{16}H_{27}NO_{10}S_2$ requires C, 42·0; H, 6·0; N, 3·1; S, 14·0%), $\nu_{max.}$ 3300m and 1550s (NH), 1750s (*O*-Ac), 1650s (*N*-Ac).

Periodate Oxidations.—The compound (15—35 mg.) was made up to 100 ml. with water including sodium metaperiodate solution and buffer, if required. The uptake of periodate was

[23] d'Ans and Frey, *Ber.*, 1912, **45**, 1845.

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determined by the neutral thiosulphate method.[24] Acid released was estimated by addition of ethylene glycol (2 ml.) to an aliquot part (5 or 10 ml.), followed by titration after 10 min. with 0·01N-sodium hydroxide to 1% w/v Methyl Red (screened with Methylene Blue).

Formaldehyde. The compound (2—5 mg.) was added to water (*ca.* 20 ml.) containing 0·2M-sodium metaperiodate (1·0 ml.), buffer (if required), and 0·1N-*p*-hydroxybenzaldehyde solution (1·0 ml.),[25] and made up to 25 ml. with water. Aliquot parts (1·0 ml.) were withdrawn and the formaldehyde liberated determined colorimetrically by the chromotropic acid method,[26] *meso*-erythritol being used as standard. Results are given in moles of either oxidant or product per mole of carbohydrate at various times (hr.).

(1) 3-Amino-1,6-anhydro-3-deoxy-β-D-altropyranose hydrochloride in unbuffered 0·024M-sodium metaperiodate.

Time	0·5	1	3	5·5	22
Uptake	1·77	1·83	1·93	2·0	2·0
Acid	0·6	0·8	0·9	1·0	0·9

(2) 3-Acetamido-3-deoxy-D-altrose in 0·01M-sodium metaperiodate at pH 3·7 (acetate buffer).

Time	0·03	0·25	0·5	1·0	2·0	4	5	7	12	24
Uptake	—	1·27	1·61	1·96	2·15	2·32	—	2·58	2·78	2·94
CH_2O	0·67	0·67	0·68	—	—	—	0·73	—	—	—

(3) D-Altrose in 0·012M-periodate at pH 3·7 (acetate buffer).

Time	0·04	0·08	0·5	2·5	4
CH_2O	0·37	0·40	0·44	0·44	0·44

(4) (2-Acetamido-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane in unbuffered 0·015M-periodate.

Time	0·25	0·75	1·5	3·0	7	24	46	73
Uptake	1·39	1·93	2·28	2·74	3·24	3·68	3·88	4·11
Acid	0·27	0·32	0·61	0·91	1·43	1·96	2·18	2·30

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[24] Neumüller and Vasseur, *Arkiv Kemi*, 1953, **5**, 235.
[25] O'Dea, *Chem. and Ind.*, 1953, 1338.
[26] O'Dea and Gibbons, *Biochem. J.*, 1953, 580.

289. *Studies with Dithizone. Part VIII.*[1] *Reactions with Organometallic Compounds.*

By H. Irving and J. J. Cox.

The published reactions of diphenylthiocarbazone (" dithizone," 3-mercapto-1,5-diphenylformazan, HDz) with organometallic compounds of arsenic, tin, lead, and mercury are reviewed. Triethyltin(IV) salts form a 1 : 1 complex, $(C_2H_5)_3SnDz$, and diethyltin(IV) chloride forms a 1 : 2 complex, Et_2SnDz_2. Trimethyl- and triphenyl-lead(IV) salts and dimethyl- and diphenyl-thallium(III) salts form highly coloured complexes R_3PbDz and R_2TlDz respectively (R = Me or Ph). Triphenyltin(IV) salts give a yellow dithizonate of composition Ph_3SnDz. All the dithizone complexes can be extracted quantitatively into an organic phase and used for the determination of the corresponding organometallic compound.

The absorption spectra of dithizone complexes of metallic and organometallic ions are discussed in relation to their structure. There appears to be a linear correlation between the wavelength of maximum absorbancy of a metal–dithizone complex and the logarithm of the stability constant of the corresponding metal–halide complex.

Diphenylthiocarbazone (" Dithizone," 3-mercapto-1,5-diphenylformazan, HDz; I or II, Ar = Ph, R = H) is widely used in trace-metal analysis since, with a limited number of metals, it forms highly coloured inner complexes which are insoluble in water but sufficiently soluble in organic solvents to lend themselves to solvent-extraction procedures.[2] The " dithizone elements " form a compact group in the centre of the Periodic Table whose limits (see Table 1) can be correlated generally with the increasing tendency of the metal to exist as a simple cation of low charge and to form metal–sulphur in preference to metal–oxygen bonds.[3]

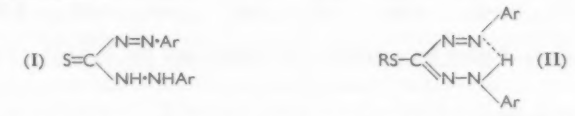


Table 1. *Elements that form well-established dithizone complexes are enclosed in continuous lines. The broken lines enclose other elements for which the evidence is less certain.*

Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se
Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te
Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po

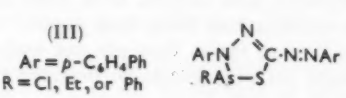
Although some of these elements (*e.g.*, copper and mercury) are said to form complexes in two valency states, tin and lead form complexes only in the bivalent state. Thallium(III) and iron(III) are said to oxidize the reagent, although their reactions have not been fully investigated.[2,4] The alleged formation of a red ruthenium complex has been contested.[2,5] Germanium(II) may form a dithizonate * capable of solvent-extraction, but germanium(IV) and gallium(III) do not.[6] Antimony(III) has been shown to form a

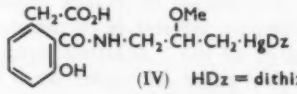
* The terms " dithizonate " and " oxinate " for complexes of metals with dithizone or oxine (8-hydroxyquinoline) are logically incorrect in that they imply that these complexes are derived from dithizonic and oxinic acid respectively. However, this terminology has become almost universally accepted and it is adopted here for the sake of uniformity.

[1] Part VII, *J.*, 1960, 1272.
[2] Iwantscheff, " Das Dithizon und seine Anwendung in der Mikro- und Spurenanalyse," Verlag Chemie, G.M.B.H., Weinheim/Bergstr., 1958.
[3] Fischer, *Mikrochem. Mikrochim. Acta*, 1942, **30**, 39.
[4] Dawson, *Analyst*, 1948, **73**, 618; Weber, *Croat. Chim. Acta*, 1957, **29**, 73.
[5] Yaffe and Voigt, *J. Amer. Chem. Soc.*, 1952, **74**, 5043; Steiger, *Mikrochem.*, 1934, **16**, 193.
[6] Irving *et al.*, unpublished results.

dithizonate which is orange-red in molten naphthalene [7] and strawberry-red in chloroform and carbon tetrachloride.[8] Dithizone has been used for the solvent extraction of tellurium(IV), ^{129}Te being used as a tracer.[9]

The very great sensitivity of dithizone as an absorptiometric reagent for traces of metals has led a number of authors to consider its application to the detection and determination of organometallic compounds. Tarbell *et al.*[10] found that di-(4-biphenylyl)thiocarbazone reacted with dichloroethylarsine in the presence of bases to give a 1 : 1 complex which they formulated as (III; R = Et). A similar compound was obtained from arsenic(III) chloride and from phenylarsenic(III) oxide, AsPhO.





(IV) HDz = dithizone

The increasing use of organotin compounds as fungicides and for the treatment of boils [11] has led to studies of their absorptiometric determination with the aid of dithizone.[12] The reagent reacts with triethyltin(IV) salts to give a strongly coloured complex ($\lambda_{max.}$ 435 mμ; ε 23,300) whose composition was not determined. From data in Aldridge and Cremer's paper [12] it is possible to calculate that it must have been the 1 : 1 complex Et_3SnDz. Salts of tri-n-propyl- and tri-n-butyl-tin(IV) are said to form dithizone complexes with spectra similar to that of the triethyltin(IV) complex. By making use of the data quoted for the interaction of diethyltin(IV) salts with dithizone [12] we deduce that a complex ($\lambda_{max.}$ 510 mμ; ε 70,500) has been formed from two molecules of dithizone and one of diethyltin(IV) salts; the probable composition is therefore Et_2SnDz_2. Dibutyl- and dioctyl-tin(IV) salts are said [12] to give dithizone complexes with similar spectra. Tetraalkyltins do not react with dithizone,[12] nor, apparently, does tetraethyl- or tetraphenyl-lead,[6,13,14] although a red compound of unknown composition is said to be formed when solid dithizone and tetraphenyl-lead are ground together.[13]

s-Butylmercury(II) bromide appears to react with dithizone, although this does not seem to have been investigated by the authors: [15] di-s-butylmercury does not react with dithizone,[15] nor does diphenylmercury.[6]

Dithizone has been used in recent procedures for the analysis of spray residues for organomercurials. The optical absorption peaks of ethylmercury(II) dithizonate and phenylmercury(II) dithizonate in 95% ethanol are reported by Webb *et al.*[16] to be at 480 mμ and at 266 and 475 mμ respectively. Miller *et al.*[17] state that the absorption spectrum of ethylmercury(II) dithizonate in chloroform resembles, but does not coincide with, that of mercury(II) dithizonate, and that ethylmercury(II) dithizonate, phenylmercury(II) dithizonate, and the complex (IV) each have an absorption maximum at 475 mμ. Gran,[18] however, reports 497 mμ for the absorption maximum of phenylmercury(II) dithizonate

[7] Carlton and Bradbury, *Analyt. Chem.*, 1954, **26**, 1226; Carlton, Bradbury, and Kruh, *Analyt. Chim. Acta*, 1955, **12**, 101.
[8] Burstall, Davies, Linstead, and Wells, *J.*, 1950, 520; Pfeifer and Diller, *Z. analyt. Chem.*, 1956, **149**, 264.
[9] Mabuchi, *Bull. Chem. Soc. Japan*, 1956, **29**, 842.
[10] Tarbell and Bunnett, *J. Amer. Chem. Soc.*, 1947, **69**, 263; Tarbell, Todd, Pauson, Linstrom, and Wystrach, *J. Amer. Chem. Soc.*, 1948, **70**, 1381.
[11] Stoner, Barnes, and Duff, *Brit. J. Pharmacol.*, 1955, **10**, 16; Aldridge and Cremer, *Biochem. J.*, 1955, **61**, 406; van der Kerk and Luitjen, *J. Appl. Chem.*, 1954, **4**, 314; Anon., *Brit. Med. J.*, 1954, **2**, 693.
[12] Aldridge and Cremer, *Analyst*, 1957, **82**, 37.
[13] Steiger, *Mikrochemie*, 1937, **22**, 216.
[14] Griffing, Rozek, Snyder, and Henderson, *Analyt. Chem.*, 1957, **29**, 190; Steiger, *Petroleum Z.*, 1937, No. 27, **33**, 3.
[15] Charman, Hughes, and Ingold, *J.*, 1959, 2530.
[16] Webb, Bhatia, Corwin, and Sharp, *J. Amer. Chem. Soc.*, 1950, **72**, 91.
[17] Miller, Polley, and Gould, *Analyt. Chem.*, 1951, **23**, 1286.
[18] Gran, *Svensk Papperstidn.*, 1950, **53**, 234.

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in chloroform. The stoicheiometric composition of these alkyl(or aryl)mercury(II) dithizone complexes has not been rigorously established in every case.

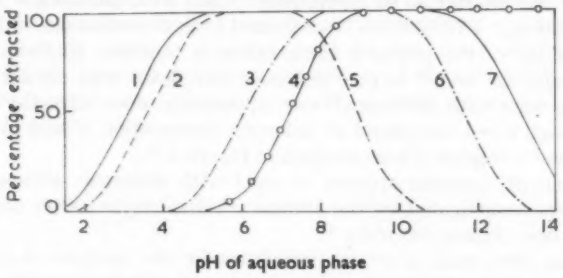
From these observations it is clear that the ions RHg^+ (R = alkyl or aryl) and R_3Sn^+ react as simple univalent cations to give RHgDz and R_3SnDz respectively, that the reactions of R_2Sn^{2+} and R_2Pb^{2+} resemble those of Sn^{2+} and Pb^{2+}, and that the inertness of R_4Sn and R_4Pb resembles that of Sn^{4+}. There seems to be little tendency for excess of dithizone to break the metal–carbon bonds and produce normal dithizone complexes such as $SnDz_2$ or $PbDz_2$.

Since the selective action of dithizone towards a limited number of metals (cf. Table 1) can clearly be extended to include organometallic ions derived from some of them, a point of immediate interest is to ascertain whether this behaviour applies to organometallic salts of all the "dithizone elements," in so far as they are not hydrolysed by water. In this paper we report some results for organometallic derivatives of thallium(III), tin(IV), and lead(IV).

Results

Solutions of dithizone in carbon tetrachloride and other organic solvents were found to react with aqueous solutions of dimethyl- and diphenyl-thallium salts and with trimethyl- and triphenyl-lead(IV) salts to give respectively red and yellow complexes which

Fig. 1. *Variation with* pH *of the percentage of various organometallic cations extracted by dithizone into carbon tetrachloride.* 1, 7, Ph_2Tl^+. 2, 5, Ph_3Pb^+. 3, 6, Me_3Pb^+. 7, Me_2Tl^+.



could be extracted quantitatively into the organic phase if the pH was adjusted within certain limits (cf. Fig. 1, and Table 2). Each complex was characterized by a very simple absorption spectrum with a well-defined peak in the visible region.

Table 2. *Extraction of dithizone complexes into carbon tetrachloride.*

Cation	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	pH range for maximum extraction
Me_2Tl^+	525	40·2	8·5 and above
Ph_2Tl^+	520	42·5	5—12
Me_3Pb^+	438	29·9	7·5—10
Ph_3Pb^+	432	31·2	5—8
Ph_3Sn^+	450	24·0	7—11

The composition of each of these new dithizonates was established by one of a variety of methods and each was found to be a 1 : 1 complex. Owing to their sparing solubility Job's method of continuous variations could not be applied to aqueous solutions. This procedure has been applied successfully to the determination of the composition of zinc dithizonate [19] by using a monophase of chloroform (20%), ethanol (70%), and water (10%), but it failed to give unequivocal results for the present complexes. Thus in a monophase buffered at pH 7·9 the absorption bands due to dithizone (455 and 595 mμ), the dithizonate ion (478 mμ), and diphenylthallium(III) dithizonate (495 mμ) overlapped

[19] Irving, Bell, and Williams, *J.*, 1952, 357.

to such an extent that the calculated Job ordinate never exceeded 0·035 and the extremum could not be located accurately.

To establish the composition of the complexes formed by the ions Me_3Pb^+ and Me_2Tl^+, a solution containing a constant known amount, C_R, of dithizone in carbon tetrachloride was equilibrated with a constant volume of an aqueous buffer containing successively increasing concentrations, C_M, of the organometallic compound. The pH was chosen, after preliminary experiments, to be within the range over which the dithizone complex was known to be quantitatively extracted. Then for a 1 cm. cell the total absorbancy of the organic phase was given by

$$A = [HDz]\varepsilon_d + [MDz_n]\varepsilon_c = C_R\varepsilon_d + C_M(\varepsilon_c - n\varepsilon_d)$$

where ε_d and ε_c were the molecular extinction coefficients of dithizone and the complex MDz_n respectively at the wavelength of measurement. The absorbancy of the organic phase increased monotonically with C_M if ε_c was greater than $n\varepsilon_d$. This was the case if

FIG. 2. *Spectrophotometric determination of the composition of the complex formed between dithizone and the trimethyl-lead*(IV) *cation.*

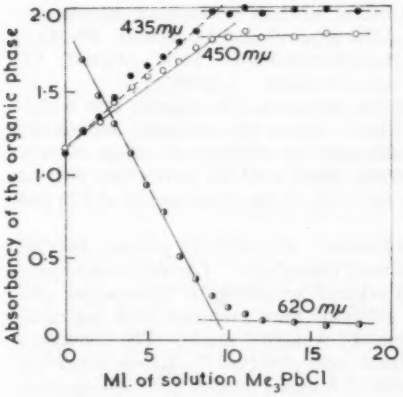
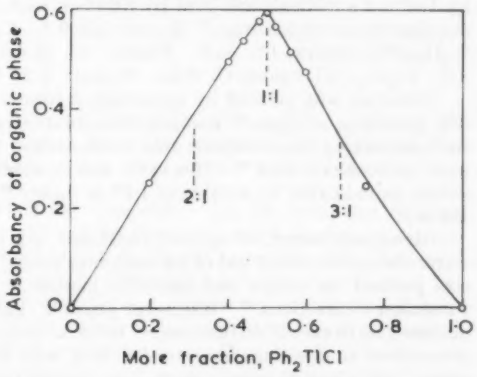


FIG. 3. *Application in a two-phase system of Job's method of continuous variations to the determination of the composition of the complex formed by dithizone with the diphenylthallium*(III) *cation.*



measurements were made at the wavelength of maximum absorption of the complex. Absorbancies measured at 620 mμ (the absorption maximum of dithizone in carbon tetrachloride where $\varepsilon_d \gg \varepsilon_c$) decreased monotonically as shown in Fig. 2. At 435 or 450 mμ where $\varepsilon_c > \varepsilon_d$, addition of the organometallic salt caused an increase in the total absorption (Fig. 2). From the volume of dithizone solution required for complete reaction, the composition of the complex could readily be calculated (cf. p. 1475).

For the diphenylthallium(III) and triphenyl-lead(IV) complexes a modification of Job's method of continuous variations was used. In this procedure the total molar concentration of the reactants is maintained constant, but the uncharged complex is extracted into a water-immiscible phase, carbon tetrachloride in the present case. As in the familiar form of Job's method,[20] some physical property of the complex is measured (in this case the absorbancy in the organic phase) and plotted against the mole ratio of the reactants. For the system diphenylthallium(III) chloride–dithizone, the graph (Fig. 3) takes the form of two straight lines whose intersection at a mole fraction of 0·5 establishes the 1 : 1 stoicheiometry of the complex. A full discussion of the theory of this form of the method of continuous variations has been given.[21]

[20] Vosburgh and Cooper, *J. Amer. Chem. Soc.*, 1941, **63**, 437.
[21] Irving and Pierce, *J.*, 1959, 2565.

The molecular extinction coefficients of the complexes were calculated by converting a known quantity of highly purified dithizone (see p. 1476) completely into the form of the desired organometallic complex and measuring its absorbancy. The concentration of the solution of pure dithizone in carbon tetrachloride was obtained from its measured absorbancy and the accurately known molecular extinction coefficient.[6,22] In the case of triphenyltin(IV), however, a graphical method was used involving measurements on a series of mixtures of dithizone and the complex (see p. 1476).

Experimental

Materials.—Samples of dimethylthallium(III) iodide, trimethyl-lead(IV) chloride, and triphenyltin(IV) chloride were recrystallized before use. Diphenylthallium(III) chloride, prepared by Meyer and Bertheim's method,[23] was recrystallized three times from pyridine, washed with hot acetone, and kept in a vacuum-desiccator over concentrated sulphuric acid to remove the last traces of base. Tetraphenyl-lead was prepared by Pfeifer's method [24] and from this triphenyl-lead(IV) chloride was made, by following the procedure of Gilman *et al.*,[25] and finally recrystallised from ethanol. Owing to the low solubility of the chloride in water, it was converted into the fluoride by Krause and Pohland's method.[26] For analyses, organic material was destroyed by wet-ashing, and boiling the sample under reflux with nitric acid for halide determinations and with perchloric acid for metal determinations. Halide ions were determined by Volhard's method, and lead by titration with a standard solution of disodium dihydrogen diaminoethanetetra-acetate [27] (Found: Cl, 9·2. $C_{18}H_{15}ClSn$ requires Cl, 9·2. Found: Pb, 45·7. $C_{18}H_{15}FPb$ requires Pb, 45·3. Found: Cl, 12·4. C_3H_9ClPb requires Cl, 12·35. Found: Cl, 9·0. $C_{12}H_{10}ClTl$ requires Cl, 8·95. Found: I, 35·1. C_2H_6ITl requires I, 34·95%).

Dithizone was purified by extracting it from a solution in carbon tetrachloride into metal-free ammonia solution,[28] washing this solution with pure carbon tetrachloride, and finally back-extracting the dithizone into fresh carbon tetrachloride by addition of excess of very pure hydrochloric acid.[28] This cycle was repeated several times until the purity was 98% or better, as indicated by a value of 1·67 or higher [22] for the ratio of the absorbancies at 620 and 450 mμ.

High-grade water, of specific resistance <2 megohms/cm., obtained by passing distilled water through a mixed bed of ion-exchange resins, was used throughout. Carbon tetrachloride was purified by Geiger and Sandell's method,[29] and ethanol according to Weissberger and Proskauer's directions.[30] Whenever possible, buffer solutions were prepared from materials obtained by isopiestic distillation; [28] other reagents were of "AnalaR" grade. The customary precautions in cleaning glassware for work with dithizone were observed.[31] Unless otherwise stated, all absorptiometric work was carried out with a Unicam model S.P. 500 spectrophotometer and matched 1 cm. silica cells. Measurements of pH were made with an Electronic Instruments Ltd. model 23 direct-reading pH meter and a Morton electrode system.

Extractibility of Organometallic Dithizonates as a Function of pH.—(a) *Trimethyl-lead*(IV) *dithizonate.* 5 ml. of a solution of dithizone in carbon tetrachloride (0·149mM) were equilibrated with 5 ml. of an aqueous solution (0·078mM) of trimethyl-lead(IV) chloride and 5 ml. of an aqueous buffer by agitation for 30 min. in a ground-glass stoppered Pyrex test-tube. When the phases had separated, the organic layer was removed and centrifuged to remove any droplets of water. The absorbancy of a portion was then measured (1 cm. cell) at 438 mμ [the wavelength previously found for the maximum absorption of the trimethyl-lead(IV) dithizonate] and also at 620 mμ, where the absorption of dithizone is maximal and that of the organometallic complex

[22] Cooper and Sullivan, *Analyt. Chem.*, 1951, **23**, 613.
[23] Meyer and Bertheim, *Ber.*, 1904, **37**, 2053.
[24] Pfeifer and Truskier, *Ber.*, 1904, **37**, 1125.
[25] Gilman and Robinson, *J. Amer. Chem. Soc.*, 1929, **51**, 3112.
[26] Krause and Pohland, *Ber.*, 1922, **55**, 1287.
[27] Schwarzenbach (trans. Irving), "Complexometric Titrations," Methuen, London, 1957, p. 92.
[28] Irving and Cox, *Analyst*, 1958, **83**, 526.
[29] Geiger and Sandell, *Analyt. Chim. Acta*, 1953, **8**, 197.
[30] Weissberger and Proskauer, "The Technique of Organic Chemistry," Oxford, 1935, Vol. VII, "Organic Solvents," p. 34.
[31] (*a*) Sandell, "Colorimetric Determination of Traces of Metals," Interscience Publ. Inc., New York, 1950; (*b*) Irving, Cooke, Woodger, and Williams, *J.*, 1949, 1847.

very small. From the latter measurement the absorption due to dithizone at 438 mμ was calculated, and subtracted from the experimental value of the absorbancy at 438 mμ. The pH of the aqueous phase was measured after equilibration. Measurements were repeated with a number of acetate, phosphate, and glycine buffers to cover a wide range of pH values.

(b) *Other organometallic dithizonates.* Similar measurements were carried out with triphenyl-lead(IV) chloride, triphenyltin(IV) chloride, dimethylthallium(III) iodide, and diphenylthallium(III) chloride, where the concentrations of organometallic ions were 0·028, 0·050, 0·081, and 0·033mM respectively, and that of dithizone 0·030, 0·048, 0·149, and 0·039mM respectively. The results are tabulated.

Trimethyl-lead(IV) *chloride.*

pH	5·22	5·91	6·30	6·86	7·17	7·82	8·40	9·64	11·09	12·65
% Extracted	18·5	44·2	57·8	76·6	85·4	97·4	100·0	100·0	71·5	12·6

Triphenyl-lead(IV) *fluoride.*

pH	3·42	4·21	4·60	4·99	5·37	5·59	5·89	6·24	6·95	7·60	8·04
% Extracted	43·0	73·0	86·7	96·4	103·4	96·5	100·0	96·2	97·4	99·4	93·1
pH	8·20	9·22	9·65								
% Extracted	83·8	33·4	22·0								

Triphenyltin(IV) *chloride.*

pH	3·40	4·05	4·63	5·37	5·89	6·24	6·95	8·04	8·79	9·98	11·14
% Extracted	0	0	12·9	41·7	72·6	98·9	102·1	100·1	103·5	99·0	95·9

Dimethylthallium(III) *iodide.*

pH	5·29	5·76	6·24	6·82	7·28	7·92	8·50	9·37	9·87	10·50	12·45
% Extracted	2·3	5·6	13·8	33·5	52·7	78·7	94·2	98·5	99·6	102·1	104·3

Diphenylthallium(III) *chloride.*

pH	3·44	4·00	4·55	4·90	5·32	5·59	5·89	6·24	6·95	7·38	7·73
% Extracted	65·9	82·6	93·1	94·9	100·7	96·9	96·6	98·7	100·2	100·3	99·6
pH		8·04	8·45	9·22	9·98	10·40	10·60	11·20	11·92	13·10	
% Extracted		100·3	101·9	101·9	97·3	98·4	98·1	101·1	93·5	50·7	

Determination of the Composition of the Dithizone Complexes.—(a) *The two-phase titration procedure.* The extractability curve for trimethyl-lead(IV) dithizonate (Fig. 1) showed it to be completely extracted into the organic phase from buffers in the pH range 7·5—10. Solutions containing x ml. of trimethyl-lead(IV) chloride (0·078 millimole/l.) and $(20 - x)$ ml. of 0·1M-boric acid–borate buffer of pH 8 were equilibrated with 5 ml. of a solution of dithizone (0·149 millimole/l.) in carbon tetrachloride. When values of the absorbancy of the separated organic phase measured at 438 mμ [the absorption maximum of trimethyl-lead(IV) dithizonate] and at 450 and 620 mμ (absorption maxima of dithizone) are plotted against the concentration of trimethyl-lead(IV) chloride (Fig. 2) a sharp change in gradient occurs when 9·2 ml. have been added, indicating the complete interaction of the components. Thus $(9{\cdot}2 \times 10^{-3} \times 7{\cdot}83 \times 10^{-5})$ mole of trimethyl-lead chloride have reacted with $(5 \times 10^{-3} \times 1{\cdot}49 \times 10^{-4})$ mole of dithizone; *i.e.*, 1 mole of trimethyl-lead chloride has reacted with 1·034 moles of dithizone, whence the stoicheiometric formula of the trimethyl-lead(IV)–dithizone complex is Me_3PbDz.

Similar measurements were carried out with dimethylthallium(III) iodide (0·081mM) and a M-ammonia–ammonium chloride buffer of pH 10, measurements being at 450, 525, and 620 mμ. In this case the ratio of dimethylthallium(III) iodide to dithizone was 1 : 0·988, confirming the formula Me_2TlDz.

(b) *The method of continuous variations applied in a two-phase system.*[21] The extractibility curve for diphenylthallium(III) dithizonate (Fig. 1) had shown the complex to be completely extracted into the organic phase in the pH range 5—12. Solutions containing x ml. of diphenylthallium(III) chloride (0·0575 millimole/l.) and $(5 - x)$ ml. of M-ammonia–ammonium chloride buffer of pH 10 were equilibrated with solutions containing $(5 - x)$ ml. of dithizone in carbon tetrachloride (0·0575mM), diluted to 5 ml. with pure organic solvent. After the phases had separated, the organic layer was removed and centrifuged:

Dithizone (mole %)...	20	40	44	48	50	52	56	60	80
Absorbancy, 520 mμ	0·245	0·475	0·515	0·566	0·596	0·578	0·538	0·495	0·249

The absorbancy at 520 mμ [the absorption maximum of diphenylthallium(III) dithizonate] was plotted against the mole fraction of organometallic salt (Fig. 3). The well-defined maximum

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at 50 moles % of diphenylthallium(III) chloride proves that the stoicheiometric formula of the diphenylthallium(III) complex is Ph_2TlDz.

The procedure was repeated with triphenyl-lead(IV) fluoride (0·028mM) and a 0·066M-phosphate buffer of pH 6·3. Absorbancies were measured at 432 mμ (the absorbancy maximum of the complex) and at 620 mμ. In this case a correction had to be made for the contribution to the absorbancy by free dithizone, but the plot clearly established the stoicheiometric formula of the triphenyl-lead(IV) complex as Ph_3PbDz.

Dithizone (mole %)...	20	30	40	45	50	55	60	70	80
Absorbancy, 432 mμ	0·235	0·277	0·364	0·410	0·444	0·460	0·483	0·525	0·567
Absorbancy, 620 mμ	0·002	0·002	0·007	0·005	0·056	0·127	0·224	0·398	0·589

Triphenyltin(IV) chloride was too insoluble in water to enable the composition of its dithizone complex to be determined in this way. Mixtures of x ml. of a 0·050mM-solution of dithizone in carbon tetrachloride with $(10 - x)$ ml. of a 0·050mM-solution of triphenyltin(IV) chloride in carbon tetrachloride were therefore equilibrated with 5 ml. of an aqueous buffer of pH 10, and the absorbancy of the organic phase measured at 450 mμ. The maximum at 50 moles % of triphenyltin(IV) chloride in the plot of absorbancy against molar composition confirmed the formula of the dithizonate as Ph_3SnDz.

Dithizone (mole %)	0	20	30	40	45	50	55	60	70	80	100
Absorbancy, 450 mμ	0·008	0·282	0·422	0·557	0·612	0·647	0·557	0·537	0·416	0·299	0·063

Determination of the Molecular Extinction Coefficients of Dithizone Complexes.—(a) *Trimethyllead*(IV) *dithizonate.* A solution of purified dithizone in carbon tetrachloride (5 ml.) was equilibrated with 5 ml. of a glycine–glycinate buffer of pH 7·8 and an excess of trimethyllead(IV) chloride crystals. The organic phase was separated, then centrifuged to remove water droplets, and its absorbancy was measured at 438 mμ. In typical results the absorbancy of the original dithizone (1 cm. cells) was 0·639 ± 0·002 at 450 mμ and 1·076 ± 0·003 at 620 mμ. From the absorbancy ratio (1·683 ± 0·003) the purity was 98·8% and the concentration 0·062mM.[32] From the absorbancy of the resulting trimethyl-lead(IV) dithizonate (0·912 ± 0·004), $\varepsilon = 29{,}320$. The average value from five determinations was $10^{-3}\varepsilon_{max.} = 29{\cdot}9 \pm 0{\cdot}9$.

(b) *Other organometallic dithizonates.* By similar procedures the following results were obtained for $10^{-3}\varepsilon_{max.}$: Ph_3PbDz, 31·2 ± 1·0; Me_2TlDz, 40·2 ± 1·1; Ph_2TlDz, 42·5 ± 1·6.

(c) *Triphenyltin*(IV) *dithizonate.* Aliquot portions (5 ml., an excess) of a solution of dithizone in carbon tetrachloride and x ml. of a standard solution of triphenyltin(IV) chloride in the same solvent were equilibrated with 5 ml. portions of a buffer of pH 10 and $(20 - x)$ ml. of water. Under these conditions the triphenyltin(IV) was completely transferred to the organic phase as its dithizonate together with excess of dithizone, whose absorbancy at 450 mμ was computed from the absorbancy at 620 mμ (where the complex transmits completely) and the known absorption spectrum of the pure reagent. The gradient of the plot of the absorbancy due to triphenyltin(IV) dithizonate alone against the concentration of organometallic salt taken gave $10^{-3}\varepsilon = 24{\cdot}0 \pm 0{\cdot}3$ as a mean of three determinations.

Discussion

Although the stoicheiometric compositions of many of the simple dithizonates have been established, their structures are still in dispute. Those suggested by Fischer[32] (*e.g.*, V; M = a bivalent metal) have been widely used (cf. Sandell[31]), but they can be criticized on many grounds.[2,31b] More probable structures involve metal–sulphur bonds.[31b,33] If, as in other compounds containing the formazan structure,[34] a mesomeric six-membered ring system is formed by hydrogen bonding, each dithizone residue could then occupy only one co-ordination position on the metal atom (as VI). In an alternative formulation (VII) a five-membered chelate ring would occupy two *cis*-co-ordination positions of the metal atom.[6,33] *X*-Ray crystallographic studies support the formulation

[32] Fischer, *Angew. Chem.*, 1934, **47**, 685; 1937, **50**, 919.
[33] Geiger, *Diss. Abs.*, 1952, **12**, 249.
[34] Irving, Gill, and (in part) Cross, *J.*, 1960, 2087, and refs. therein.

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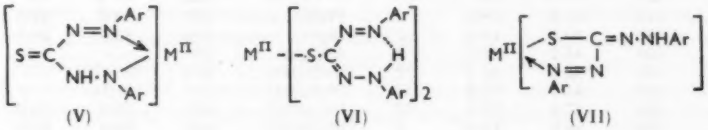
(VII) for solid mercury(II) dithizonate,[35] but this need not be taken as conclusive evidence that the alternative structure (VI) is not preferred in a solution of the complex in an organic solvent; nor are there any grounds for asserting that all metal dithizonates will adopt the same configuration. However, it would surely be expected that the absorption spectrum of a complex containing the highly symmetrical hydrogen-bonded formazan ring system (as VI) would differ from one containing the chelated structure (VII).



(V) (VI) (VII)

In simple formazans, isomerism about –N=N– and >C=N– bonds could lead to four configurational isomers, and two conformations have even been postulated for the hydrogen-bonded isomer (as VI).[36] Equilibrium between the various isomers is known to depend on the nature of the solvent and on the conditions of irradiation, and the kinetics of equilibration have been studied in considerable detail.[37] Although *cis-trans*-isomerism in solutions of *S*-methyldithizone (3-methylthio-1,5-diphenylformazan; II, R = Me) has been observed,[38] and the relative intensity of absorption of dithizone (and its analogues) in various solvents at the two maxima in the visible region (*ca.* 450 and 620 mμ) has been correlated with the position of thiol–thione equilibrium,[6] no time-dependent change in the spectrum of dithizone or of any metal dithizonate has ever been observed. [The reversible photoisomerization of mercury(II) dithizonate is a special phenomenon.] From this we conclude, either that the metal dithizonates exist in solution in a single configuration, or that there is very labile equilibrium between all possible forms.

In the formally uncharged complexes R_2SnDz and R_2SnDz_2 the metal atom can achieve its maximum co-ordination of four by forming respectively one or two metal–sulphur bonds. Further co-ordination is unlikely and chelation by the dithizone residue (as VII) cannot take place. Such complexes must be formulated as (VI) or as some variant in which the hydrogen bond is broken and the groups attached to the carbon atom (position 3) adopt one or other of several possible configurations which, for reasons advanced above, must be in labile equilibrium. On the other hand, in the complexes $SnDz_2$ and $PbDz_2$ formed by the simple ions Pb(II) and Sn(II) the dithizonate ion must act as a bidentate ligand if chelation is to bring the co-ordination number to four, although it is possible that two co-ordination positions might be occupied by water molecules. However, the latter seems improbable, for in the case of mercury(II) dithizonate [35] pyridine of crystallization is attached to the dithizone residue by hydrogen bonding, rather than co-ordinated to the metal; since pyridine is the stronger donor it seems unlikely that water should co-ordinate to the metal where pyridine fails to do so. Chelation of the type (VII) would thus be predicted for the zinc, copper, nickel, and cadmium complexes, MDz_2. Although in view of the characteristic " step " in the formation curves of many mercury complexes with monodentate ligands at $\bar{n} = 2$, mercury might have been exceptional in retaining a covalency of two in $HgDz_2$, it is found to assume a deformed tetrahedral quadricovalent configuration [35] involving nearly collinear metal–sulphur bonds with bidentate chelate rings completed through nitrogen atoms of the formazan residues.

The available spectrophotometric data (Table 3) reveal no uniform pattern of behaviour and we can find no correlation between the wavelength or intensity of absorption of individual dithizonates and the electronic structure of the cation from which they are

[35] Harding, *J.*, 1958, 4136.
[36] Busch and Schmidt, *J. prakt. Chem.*, 1931, **131**, 182; Ragno and Oreste, *Gazzetta*, 1948, **78**, 228.
[37] Hausser, Jerchel, and Kuhn, *Chem. Ber.*, 1949, **82**, 515; Kuhn and Weitz, *ibid.*, 1953, **86**, 1199.
[38] (*a*) Irving and Bell, *J.*, 1954, 4253; (*b*) Ferguson, B.Sc. Thesis, Oxford, 1957.

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derived. The only common feature is the strong absorption band in the visible region between 432 and 550 mμ ($10^{-3}\varepsilon = 8$—46 per unit of dithizone); weaker bands ($10^{-3}\varepsilon =$ 12—19 per unit of dithizone) occur in the near ultraviolet region ($\lambda_{max.}$ 265—280). Complexes of nickel(II), palladium(II), platinum(II), and gold(III) are exceptional in showing

TABLE 3. *Absorption spectra of dithizone complexes in carbon tetrachloride.*

Cation	$\lambda_{max.}$	$10^{-3}\varepsilon$	ex.[b]	Ref.	Cation	$\lambda_{max.}$	$10^{-3}\varepsilon$	ex.[b]	Ref.
Co(II)	542	59·2	29·6	2	Pb(II)	520	68·6	34·3	22
Ni(II)	480	30·4	15·2	2	Bi(III)	490	80·0	26·7	2
Cu(II)	550	45·2	22·6	2	AsCl(III) ...	460	—	—	10
Zn(II)	535	92·6	46·3	22	AsEt(III) ...	510	*ca.* 37	—	10
Pd(II)	450	34·4	17·2	2	PhAs(III) ...	510	*ca.* 34	—	10
Ag(I)	462	27·2	27·2	22	Et_2Sn(IV) ...	438	23·2	23·2	12
Cd(II)	520	88·0	44·0	2	Ph_3Sn(IV) ...	450	23·9	23·9	*a*
In(III)	510	87·0	29·0	2	Et_3Sn(IV) ...	506	70·5	35·3	12
Sn(II)	520	54·0	27·0	2	Me_2Pb(IV)...	438	29·9	29·9	*a*
Pt(II)	490	31·6	15·8	2	Ph_2Pb(IV)...	432	31·2	31·2	*a*
Au(III)	450	31·6	10·5	2	Me_2Tl(III) ...	525	40·2	40·2	*a*
Hg(II)	485	70·0	35·0	22	Ph_2Tl(III) ...	520	42·5	42·5	*a*
Tl(I)	510	33·2	33·2	2					

[a] Present work. [b] The figures in cols. 4 and 9 headed " ex." are values of $10^{-3}\varepsilon$ divided by the number of molecules of dithizone in each complex.

weaker absorption throughout the visible region with broad overlapping maxima of comparable intensity between 640 and 710, 450 and 490, and 260 and 282 mμ.

It has been pointed out [39] that for complexes of 8-hydroxyquinoline with a number of uni-, bi- and ter-valent cations the molecular extinction coefficient divided by the number of oxine residues is substantially constant ($10^{-3}\varepsilon$ 2·24 ± 3%) irrespective of the nature or valency of the cation. By contrast, individual values of $10^{-3}\varepsilon$ for dithizonates vary from 92·6 for zinc dithizonate to 23·2 for triethyltin(IV) dithizonate. Even after recalculation on the basis of the number of dithizone residues involved Fig. 4 (Table 3), the variations are still very large (30,000 ± 50%) and demonstrate clearly the specific effects of different metals in modifying transition probabilities in the absorbing species. The wide range of values also supports the suggestion that the configuration of the ligand [*e.g.*, as (V), (VI), or (VII)] is unlikely to be the same for all metal dithizonates. A comparison with the spectrum of *S*-methyldithizone [38a] (II; R = Me) is suggestive, for this substance cannot possibly contain the ring systems postulated by structures (V) or (VII): it is perhaps significant that the molecular extinction coefficient is very low (10,000).

Some regularities in the effect of substitution on spectra may be noted: (*a*) The addition of alkyl groups without change of net charge [Sn(II) to Ph_2Sn(IV); Tl(I) to Me_2Tl(III)] increases the intensity of absorption. (*b*) The addition of alkyl groups with concurrent decrease in charge provokes a decrease in molecular extinction coefficient [*e.g.*, Sn(II) to Et_3Sn(IV); Pb(II) to Me_3Pb(IV)]. (*c*) Replacement of Me (or Et) by Ph causes an increase in $\varepsilon_{max.}$ which is small for tin ($\Delta\varepsilon$ +700), large for lead ($\Delta\varepsilon$ +1300) and thallium ($\Delta\varepsilon$ +2300), and very large for mercury ($\Delta\varepsilon$ +8400 to 16,300).[6]

We have recently commented [40] on the fact that the small number of simple cations that react selectively with dithizone to form complexes are generally those of class (*b*) metals, *i.e.*, those for which the stability of their halide complexes increases in the order $F^- \ll Cl^- < Br^- < I^-$. It was further noted that the absorption maximum of the metal–dithizone complex shifts towards shorter wavelengths as the strength of the metal–chloride (bromide or iodide) bond increases. There is a roughly linear relation between $\lambda_{max.}$ and $\log_{10} K$, where K is the stability constant of the 1 : 1 complex (Ref. 40, Fig. 2). There are no data for the strengths of the metal–ligand bonds in any dithizone complexes, but in so far as d_π–p_π bonding is equally effective in reinforcing the strength of σ-bonds between a

[39] Irving and Williams, *Analyst*, 1952, **77**, 813.
[40] Irving and Cox, *Proc. Chem. Soc.*, 1959, 324.

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class (*b*) metal and chlorine (bromine or iodine) and a class (*b*) metal and sulphur, it is reasonable to expect that the hypsochromic shift is associated with a stronger bond between the metal and the ligand, it being always assumed that this is bonded through a sulphur atom. Increase of valency (in the present case by the loss of an inert pair of electrons) will reduce the radius of a metal ion and favour d_π–p_π overlap. This may account for the hypsochromic effect in the series Pb(II) [520 mμ ⟶ Me_3Pb(IV) (438 mμ) or Ph_3Pb(IV) (506 mμ)]; Sn(II) [(520 mμ) ⟶ Et_2Sn(IV) (506 mμ) or Et_3Sn(IV) (438 mμ) or Ph_3Sn(IV) (450 mμ)], where, for reasons stated above it seems likely that co-ordination through sulphur atoms is not accompanied by the formation of a chelate ring. In the series Tl(I) ⟶ Me_2Tl(III) (525 mμ) or Ph_2Tl(III) (520 mμ), where there is a small bathochromic effect, the preservation of a co-ordination number of four must involve co-ordination through both sulphur and nitrogen (or, in the case of the thallous ion, oxygen from water as well).

It will be apparent that the interpretation of the spectra of metal dithizonates is far from complete, and the hope of being able to use differences in spectra to distinguish between alternative structures has not been realized. However, the distinctive spectra and high molecular extinction coefficients of the different organometallic dithizonates, coupled with their characteristic pH range for extraction, can form the basis for a variety of analytical determinations and separations which will be described elsewhere.

Thanks are offered to Dr. J. Prue (Reading University) for the gift of dimethylthallium(III) iodide and to Dr. B. C. Saunders (Cambridge University) for the gift of trimethyl-lead(IV) chloride. We are indebted to the Royal Society for the loan of a Unicam S.P. 700 recording spectrophotometer, and one of us (J. J. C.) gratefully acknowledges financial support from the Department of Scientific and Industrial Research.

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290. *The Radiation Chemistry of Azide Solutions. Part I. The Action of X-Rays* (200 kv) *on Deærated Aqueous Solutions of Sodium Azide.*

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The principal products produced in the radiolysis (200 kv *X*-rays) of aqueous solutions of sodium azide at pH 8·0, in the absence of oxygen, are nitrogen and ammonia, the yields of which vary markedly with the azide concentration.

The results have been shown to be accommodated by a mechanism in which both the oxidising and the reducing species produced by the interaction of the ionising radiation with water react with the azide ion, leading to the N_3 radical and to nitrogen and the NH^- ion, respectively. The N_3 radical has been found to be stable with respect to its self-dissociation.

INVESTIGATIONS on the chemical effects of ionising radiations in deærated dilute aqueous solutions have mainly been confined to acidic solutions (pH 0—2·5). It has been found [1] that a satisfactory account of both organic and inorganic systems, in this pH range, can be given on the basis of the two primary processes:

$$H_2O \longrightarrow H + OH \quad \ldots\ldots\ldots\ldots\ldots (1)$$

$$2H_2O \longrightarrow H_2 + H_2O_2 \quad \ldots\ldots\ldots\ldots\ldots (2)$$

As the pH is increased, however, the hydrogen yields from organic solute systems decrease markedly,[2] as is not expected in terms of reactions (1) and (2).

[1] Allen, *Radiation Res.*, 1954, **1**, 85.
[2] Jayson, Scholes, and Weiss, *J.*, 1957, 1358.

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After a theoretical discussion by Weiss,[3] Hayon and Weiss,[4] and Weiss [5] produced some evidence that the H_2O^+ and particularly H_2O^-, formed in the primary process by the ionising radiations, may under suitable conditions be sufficiently stable to enter directly into chemical reactions. Particular interest attaches to what is denoted as the H_2O^- ion, the "polaron," *i.e.*, an electron moving around in the water accompanied by its cloud of polarisation.[3] In the following, this is written as H_2O^-, which denotes here a "polaron" and not a negatively charged water molecule.

On this basis the formation of hydrogen atoms is due to:

$$H_2O^- + H_3O^+ \longrightarrow H + 2H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

This reaction leads to pH-dependence of the hydrogen yield if a suitable solute is present to accept the H_2O^-. Allan and Scholes [6] have given a quantitative account of the pH-dependence of the radiolysis of aqueous propan-2-ol, in terms of reaction (3). Studies of the radiolysis of aqueous solutions of methanol and ethanol [7] also indicate the validity of reaction (3). We show now that the azide ion is a suitable inorganic solute capable of accepting this polaron. In the following paper, confirmation of this is obtained in a study of the irradiation of mixtures of sodium azide and various organic compounds.

Results

In order to avoid the presence of hydrazoic acid [8] ($K \sim 2 \times 10^{-5}$) all experiments were carried out at pH 8·0. This was satisfactory, for (*a*) no loss of sodium azide occurred during the evacuation, (*b*) no hydrazoic acid was detectable, after irradiation, in the gas-phase products, and (*c*) the yields were independent of the buffer concentration.

Solutions of 10^{-3}M- and 10^{-1}M-sodium azide were irradiated *in vacuo* with various doses and tested for ammonia, hydrazine, hydrogen peroxide, nitrite, nitrate, and hydroxylamine. The only gaseous products detectable were nitrogen, hydrogen, and nitrous oxide.

With 10^{-3}M-sodium azide the only detectable products in solution were ammonia and nitrite, but the yield of nitrite was virtually negligible ($G \sim 0{\cdot}02$) as was that of nitrous oxide ($G \sim 0{\cdot}003$). Up to total doses of 6×10^{-6} ev/N per ml., the yields of ammonia, nitrogen,

Table 1. *Dependence on azide concentration of the initial yields of products in the irradiation of deærated solutions of sodium azide with* X-*rays* (200 kv).

	Yields (G values) of				
Azide concn. (M)	N_2	H_2	N_2O	NH_3	Azide depletion
1·0	12·5	0·5	0·4	2·9	—
0·5	11·3	0·55	0·35	2·7	—
0·25	10·9	0·60	0·30	2·4	—
0·1	10·2	0·60	0·20	2·0	—
0·01	6·9	0·70	0·01	1·0	—
0·001	4·4	0·70	Negligible	0·65	3·1
Average % deviation from mean G value	±2	±2	±5	±7	±6

and hydrogen were linear functions of dose, namely, $G(N_2) = 4{\cdot}4$, $G(NH_3) = 0{\cdot}65$, $G(H_2) = 0{\cdot}7$ (Table 1). The depletion in azide over the same range of dose was also found to be a linear function of dose, with $-G(N_3^-) = 3{\cdot}1$, in agreement with the values of $G(N_2)$ and $G(NH_3)$.

With 10^{-1}M-sodium azide the products in solution were again only ammonia and nitrite although the yield of both was considerably increased: $G(NH_3) = 2{\cdot}0$, $G(NO_2^-) = 0{\cdot}1$.

The initial yields of nitrogen, hydrogen, nitrous oxide, and ammonia were measured at

[3] Weiss, *Ann. Rev. Phys. Chem.*, 1953, **4**, 143; *Experientia*, 1956, XII/7, 280.
[4] Hayon and Weiss, Proc. 2nd Internat. Conference on the Peaceful Uses of Atomic Energy, Geneva, 1958.
[5] Weiss, *Nature*, 1960, **186**, 751.
[6] Allan and Scholes, *Nature*, 1960, **187**, 218.
[7] Lyon, Nixon, Scholes, and Smith, unpublished results.
[8] Yui, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1941, **20**, 390.

various concentrations of azide. ("Initial yields" is a somewhat arbitrary term and here represents yields for total doses in the range 0·8—3·5 × 10^{-6} ev/N per ml., this dose range being chosen because it represents the practical limits of detection of ammonia.) The difficulties of separation of hydroxylamine and nitrate were such that, in this initial yield dose range, a

FIG. 1. *Dependence on azide concentration of the initial yields of nitrogen in the irradiation of deærated aqueous solutions of sodium azide with X-rays* (200 kv).

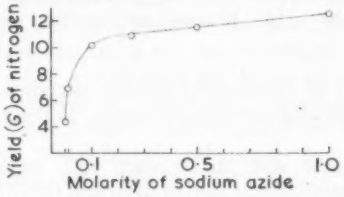


FIG. 2. *Dependence on azide concentration of the initial yields of ammonia in the irradiation of deærated solutions of sodium azide with X-rays* (200 kv.)

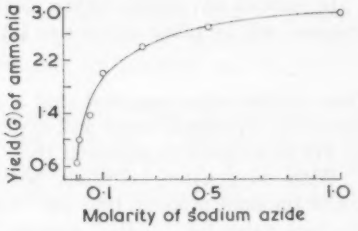


FIG. 3. *Dependence on azide concentration of the initial yields of nitrous oxide in the irradiation of deærated aqueous solutions of sodium azide with X-rays* (200 kv).

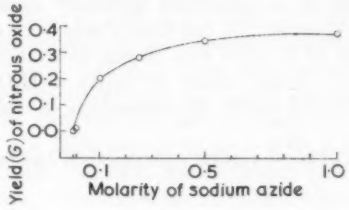
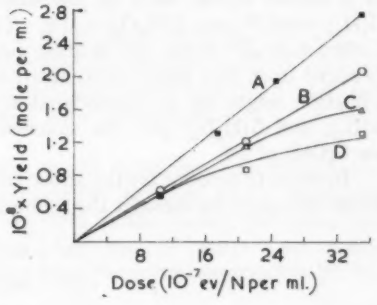


FIG. 4. *Formation of ammonia* (A), *hydrogen* (B), *nitrous oxide* (C), *and oxygen* (D) *in the irradiation of deærated aqueous solutions of sodium azide* (10^{-1}M) *in the presence of hydrogen peroxide* (10^{-4}M) *with X-rays* (200 kv).



negative test did not preclude their formation up to a value of $G \sim 0{\cdot}2$. In all cases the dose–yield curves were linear and the results in Figs. 1—3 are the mean values of at least three separate experiments.

Irradiations were also carried out in the presence of oxygen, at 10^{-3}M-azide only. Hydrogen peroxide was the only measurable product in solution. The dose–yield curves for the depletion of azide and the production of hydrogen peroxide, in oxygen-saturated solutions, were linear up to doses of 14 × 10^{-6} ev/N per ml., giving $-G(N_3^-) = 0{\cdot}9 \pm 0{\cdot}1$, and $G(H_2O_2) = 0{\cdot}9 \pm 0{\cdot}1$.

TABLE 2. *Dependence on azide concentration of the initial yields of products in the irradiation of deærated solutions of sodium azide in the presence of hydrogen peroxide* (10^{-4}M) *with X-rays* (200 kv).

	Yield (G values) of					
Azide concn. (M)	N_2	H_2	N_2O	O_2	NH_3	Depletion of H_2O_2
0·1	5·4	0·6	0·6	0·54	0·8	2·1
0·05	4·5	0·6	0·55	0·50	0·4	2·2
0·01	—	—	—	—	0·1	2·2
0·001	3·0	0·7	0·4	0·95	0·0	2·4
Average % deviation from mean G value	±2	±2	±5	±5	±7	±5

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A few examinations were made of those gas-phase products which were condensable in liquid oxygen: the only detectable product was nitrous oxide to an extent of $G \sim 0{\cdot}2$.

The presence of 10^{-4}M-hydrogen peroxide in the irradiation of 10^{-1}M-azide decreased the yield of nitrogen [$G(N_2) = 5{\cdot}4$] and ammonia [$G(NH_3) = 0{\cdot}8$], increased that of nitrous oxide, and led to a new product, *viz.*, oxygen (Fig. 4). Similar results were obtained at other azide concentrations (Table 2).

Discussion

In view of the results of the alcohol studies mentioned above, the primary chemical processes will be taken as reaction (2) (the " molecular yield " process) and reaction (4):

$$2H_2O \longrightarrow H_2O^+ + H_2O^- \quad (4)$$

These studies also suggested that a certain number of water molecules are decomposed directly to hydrogen atoms and hydroxyl radicals, throughout the pH range; so reaction (1) will be retained to represent these.

With oxygenated solutions both hydrogen atoms and H_2O^- react with oxygen to give the same product, thus the " $G(H)$ " value obtained is the sum of $G(H)$ and $G(H_2O^-)$. The best value for " $G(H)$ " appears [9] to be 2·8 and as $G(H)$ from the alcohol studies is 0·5 (this value is for γ-rays and for the present it will be assumed that X-rays give the same), this gives $G(H_2O^-)$ 2·3. From the discussion that follows it will be seen that both hydrogen atoms and H_2O^- seem to react with the azide ion in the same manner, so it appears irrelevant here to distinguish between them. However, in Part II it will be shown that they may be differentiated by irradiating sodium azide in the presence of a second solute, such as methanol. The " molecular yields " have been taken as $G(H_2) \sim 0{\cdot}6$,[10] and $G(H_2O_2) \sim 0{\cdot}8$. The last value is a somewhat arbitrary choice. Collinson *et al.*[11] found the limiting value for $G(H_2O_2)$ to be 1·0, but that it was very dependent upon the solute concentration. The value of $G \sim 0{\cdot}8$ was chosen so that this variation might be accommodated to some extent. These values for $G(H)$, $G(H_2O^-)$, $G(H_2)$, and $G(H_2O_2)$ give, on stoicheiometric balance of water decomposition, a value for $G(OH)$ of 2·4.

In order to account for the above results in terms of these primary processes it has been found necessary to consider the following reactions:

$$OH + N_3^- \longrightarrow N_3 + OH^- \quad (5)$$

$$H_2O^- + N_3^- \longrightarrow N_2 + NH^- + OH^- \quad (6)$$

$$H + N_3^- \longrightarrow N_2 + NH^- \quad (6a)$$

$$H_2O^- + H_2O_2 \longrightarrow OH + OH^- + H_2O \quad (7)$$

$$H_2O^- + N_2 \longrightarrow N_3^- + H_2O \quad (8)$$

$$H + N_2 \longrightarrow (HN_2) \rightleftharpoons N_3^- + H^+ \quad (8a)$$

$$2N_3 \longrightarrow 3N_2 \quad (9)$$

$$NH^- + H_2O \longrightarrow NH_2 + OH^- \quad (10)$$

$$NH_2 + N_3^- \longrightarrow NH_2^- + N_3 \quad (11)$$

$$NH_2 + H_2O^- \longrightarrow NH_2^- + H_2O \quad (12)$$

$$NH_2 + H \longrightarrow NH_3 \quad (12a)$$

$$NH_2^- + H_2O \longrightarrow NH_3 + OH^- \quad (13)$$

$$N_3 + H_2O_2 \longrightarrow N_2 + NOH + OH \quad (14)$$

$$2NOH \longrightarrow N_2O + H_2O \quad (15)$$

[9] Allen and Schwarz, ref. 4, in the press.
[10] Johnson and Weiss, *Proc. Roy. Soc.*, 1957, *A*, **240**, 189.
[11] Collinson, Dainton, and McNaughton, *Trans. Faraday Soc.*, 1957, **53**, 357.

The azide ion has many properties in common with the halide ions and it has been suggested [12] that its electron affinity lies between those of the bromide and the chloride ion. If the N_3 radical is stable with respect to self-dissociation, then it will also have properties lying between those of the chlorine and the bromine atom. On this basis, reactions (5), (8), (8*a*), and (9) are plausible. From other studies, reaction (7) has been found to occur rapidly. Reactions (10) and (13) are to be expected on energetic grounds and have already been suggested by Heal.[13] Reaction (11) is considered feasible, as NH_2 is isoelectronic with the hydroxyl radical. Reaction (15) seems the most likely route of formation of nitrous oxide,[14] and reaction (14) is favourable energetically.[15] Reaction (12*a*) has been found in the photolysis of ammonia.[16] Equation (6) is merely a formal representation of the stoicheiometry of the polaron–azide ion reaction, and it is not to be taken as indicating the actual mechanism.

Reaction at Low Azide Concentrations (10^{-3}M) —It is assumed that the polaron reacts very much faster with hydrogen peroxide than with the azide ion. Consequently, at low azide concentrations, the molecular yield of hydrogen peroxide (G 0·8) is removed *via* reaction (7). The hydroxyl radical [G(OH) 2·4] is thought to react *via* (5), and likewise the hydroxyl radicals (G 0·8) formed by reaction (7).

$G(NH_3) = 0{\cdot}65$, and it is believed that reactions (6), (6*a*), followed by (12), (12*a*) are responsible for this. The rest of the polaron and hydrogen-atom yield (G 0·7) {G 2·8 — G 0·8 [the polarons and hydrogen atoms utilised in (7)] — G 1·3 (those responsible for ammonia production)} is assumed to be removed by the back reaction (8), (8*a*).

The N_3 radicals are assumed to be stable with respect to self-dissociation, so that those formed in the above reaction sequences yield nitrogen *via* (9). The total nitrogen yield is then:

$$G(N_2) = 2{\cdot}4N_3\ (5) + 0{\cdot}8N_3\ [(7) \text{ followed by } (5)] + 0{\cdot}65N_2\ (6) - 0{\cdot}7N_3\ (8) = 4{\cdot}4N_2$$

(The numbers in parentheses represent the reactions responsible for production of nitrogen or the N_3 radical.) This value agrees with the experimental figure of $G(N_2) = 4{\cdot}4$, and the above sequence of reactions is also in agreement with the absence of any products other than nitrogen and ammonia.

The hydrogen yield ($G = 0{\cdot}70$) is sufficiently close to the molecular yield to be taken as such. In fact, the hydrogen yields at all concentrations are close to the molecular yields. The decrease to values below the molecular yield at the higher concentrations is similar to that found with other inorganic solutes. Following Schwartz,[17] we ascribe this to the scavenging by the azide ion of the species from the tracks responsible for the molecular yield hydrogen formation.

Reactions at High Azide Concentrations (1·0M).—At this concentration it is assumed that all the H_2O^- and hydrogen atoms react *via* (6) and that all the NH^- is consumed *via* (10), (11), and (13). The hydrogen produced at this azide concentration is less than the accepted molecular yield value, so the deficit is taken as reacting *via* (6). Thus $G(NH_3)$ from reactions (6), (10), and (11) should be $2{\cdot}8 + 0{\cdot}2 = 3{\cdot}0$.

The "molecular yield" hydrogen peroxide is presumed to be removed by reaction (14), thus $G(N_2O)$ should be 0·4. All the N_3 radicals produced in the above reaction sequence, other than those which participate in the hydrogen peroxide reaction (14), are assumed to lead to nitrogen *via* (9). According to this scheme the total nitrogen yield should be:

$$G(N_2) = 2{\cdot}4N_3\ (5) + 3{\cdot}0N_2\ (6) + 3{\cdot}0N_3\ (10, 11) + 0{\cdot}8N_2\ (14) + 0{\cdot}8N_3\ (14, 5) - 0{\cdot}8N_3\ [N_3 \text{ from } (5) \text{ diverted to } (14)] = 11{\cdot}9N_2$$

[12] Weiss, *Trans. Faraday Soc.*, 1947, **43**, 119.
[13] Heal, *Canad. J. Chem.*, 1953, **31**, 1153.
[14] Sneed and Brasted, "Comprehensive Inorganic Chemistry," Van Nostrand, 1956, V, 57.
[15] Uri, *Chem. Rev.*, 1952, **50**, 441.
[16] Rollefson and Burton, "Photochemistry and the Mechanism of Chemical Reactions," Prentice-Hall, 1946, p. 181.
[17] Schwarz, *J. Amer. Chem. Soc.*, 1955, **77**, 4960.

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Thus the above reaction sequence agrees with the experimental figures of $G(NH_3) = 2{\cdot}9$, $G(N_2O) = 0{\cdot}4$, $G(N_2) = 12{\cdot}5$.

At the intermediate concentrations the yields will depend on the relative rates of the various reactions. It is thought likely that in 0·1M-azide, none of the H_2O^- reacts with hydrogen peroxide, the yield of ammonia being less than G 2·8 because of interaction between the NH_2 radicals and hydrogen peroxide (16):

$$NH_2 + H_2O_2 \longrightarrow NH_3 + HO_2 \quad \ldots \quad (16a)$$
$$NH_2 + H_2O_2 \longrightarrow NH_2{\cdot}OH + OH \quad \ldots \quad (16b)$$

Reaction (16*b*) leads directly to a reduction in the ammonia yield. Reaction (16*a*) will also lead to a decrease in the ammonia yield, as the HO_2 will probably lead to the formation of NH_2O_2 *via* reactions (19) and (17)

$$NH_2 + O_2 \longrightarrow NH_2O_2 \quad \ldots \quad (17)$$

The small yield of nitrite ($G \sim 0{\cdot}1$) found at this azide concentration can be accounted for in terms of (16*a*) and (17), as NH_2O_2 is a likely precursor of nitrite.[18]

If reaction (16) is correct, then the slow increase in nitrogen and ammonia between 0·1M- and 1·0M-azide is a result of reaction (11) competing with (16). The release of hydrogen peroxide from reaction (16) then enables reaction (14) to proceed more effectively, resulting in an increase in nitrous oxide, as observed.

Reactions in the Presence of Oxygen (10^{-3}M-*Sodium Azide*).—It is seen that the presence of oxygen markedly reduces the extent of azide decomposition. As reaction (5) should proceed whether or not oxygen is present, the extent of azide depletion should be at least G 2·4. The experimental figure of G 0·9 suggests therefore that a considerable amount of back-reaction ensues, probably as:

$$H_2O^- + O_2 \longrightarrow O_2^- \quad \ldots \quad (18)$$
$$H + O_2 \longrightarrow HO_2 \rightleftharpoons H^+ + O_2^- \quad \ldots \quad (18a)$$
$$O_2^- + N_2 \longrightarrow N_2^- + O_2 \quad \ldots \quad (19)$$

The yield of nitrous oxide, G 0·2, found experimentally, can be accounted for in terms of reaction (14) going to an extent of a G 0·4. If a G 0·6 of hydrogen peroxide is produced *via* the reaction (20), then, on use of the same values for the water decomposition as before, this leads to a value of 0·8 for $-G(N_3^-)$ and 1·0 for $G(H_2O_2)$ which compare well with the experimental figures of $-G(N_3^-) = 0{\cdot}9$, $G(H_2O_2) = 0{\cdot}9$.

$$2O_2^- \longrightarrow O_2^{2-} + O_2 \quad \ldots \quad (20)$$

Some confirmation for the suggestion that the nitrous oxide is formed *via* reaction (14) was given by an experiment carried out in the presence of hydrogen peroxide (10^{-4}M) in which the nitrous oxide yield increased to G 0·44.

Reactions in the Presence of Hydrogen Peroxide.—The addition of hydrogen peroxide before the irradiation of 0·1M-azide is seen to result in a decrease in the yields of ammonia and nitrogen. At the same time the yield of nitrous oxide is considerably increased and oxygen is formed. These changes in ammonia and nitrous oxide yields would be expected on the basis of, and so lend support to, reactions (14) and (16). At lower concentrations of azide, reaction (7) would be expected to compete with (6), resulting, as found, in an absence of ammonia. However, the increased number of hydroxyl radicals, produced *via* (7), should lead to at least a slight increase in the nitrogen yield, and certainly not to a decrease as observed. The increasing yield of oxygen suggests that this is possibly due to interaction of the hydroxyl radicals with the hydrogen peroxide, as:

$$OH + H_2O_2 \longrightarrow H_2O + HO_2 \quad \ldots \quad (21)$$

[18] Rigg, Scholes, and Weiss, *J.*, 1952, 3034.

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In view of the difficulties of analysis of nitrogen–oxygen compounds, and our lack of knowledge as to their reactivity, no attempt was made to amplify these preliminary experiments.

The ultraviolet band of the azide ion is very similar to that of the iodide ion,[12] and consequently has been interpreted in terms of an electron transfer to water.[19] Unlike the case of the iodide ion, however, considerable photochemical decomposition takes place in neutral and alkaline conditions.[20] It has also been found that the hydrogen forms only 2% of the gaseous products,[21] the rest being nitrogen. It seems reasonable to suppose that these results can be ascribed to the operation of reaction (6). Further support for reaction (6) comes from the fact that sodium azide solutions are reduced by alkaline sodium amalgam,[22] the main products being nitrogen and ammonia.

Experimental

X-Ray irradiations were carried out by using a Victor Maximar set operating at 200 kv and 15 ma. The Pyrex irradiation vessels, incorporating a large gas space, gave dose rates in the region of $3{\cdot}5 \times 10^{-7}$ ev/*N* per ml. per min., for the 100 ml. samples normally used, as measured by the ferrous sulphate dosimeter, the value of 15·5 being used for $G(Fe^{3+})$.[23]

Triply distilled water was used throughout the work, both for preparation of solutions and analysis of products. It was obtained by distilling ordinary distilled water from potassium permanganate and then from phosphoric acid.

All chemicals used were of "AnalaR" grade, with the exception of the sodium azide itself, which was purified by successive recrystallisations from triply distilled water. The sodium azide solutions were buffered at pH 8, by a 10^{-3}M Sörensen buffer.[24]

Evacuation and Gas Collection.—The apparatus used for evacuation and degassing of solutions and for collection and measurement of the gaseous products was similar to that used previously in these laboratories.[25] Satisfactory deæration was achieved by an initial evacuation followed by alternative vigorous shaking and connection to the vacuum-system for a very short period. Evacuated unirradiated solutions were subjected to the gas-collection procedure, and subsequent measurement of the gas volume confirmed the efficiency of the evacuation method.

The gaseous irradiation products were collected *via* a solid carbon dioxide–acetone trap, in a gas-burette capable of handling up to 30 c.c. of gas at S.T.P. Thorough shaking of the vessel before attachment to the collection system was not sufficient to ensure complete removal of the gas. After the first collection, a second shaking was necessary to liberate the remainder of the gas from the solution. The withdrawal of gas was effected by a Toepler pump and the procedure was monitored by a Pirani gauge. After measurement of its volume, the gas was transferred to a sample vessel for subsequent analysis by a Metropolitan-Vickers M.S.2. mass spectrometer.

Mass-spectrometric Analysis.—The gaseous products were hydrogen, nitrogen, and nitrous oxide together with carbon dioxide (present in the unirradiated solution) and small amounts of air. This mixture presented no difficulties in analysis. Conservative estimates of the accuracy of the analyses are: nitrogen ± 2·0 moles% in the presence of "air" nitrogen; hydrogen, ±0·5 mole%; and nitrous oxide, ±0·1 mole% in the presence of carbon dioxide.

Analysis of Products in Solution.—Determination of azide depletion. It was only in the region of 10^{-3}M-azide that $-G(N_3^-)$ could be measured; at higher concentrations the % depletion of azide was too small to be detected. Satisfactory results were obtained by using two different methods:

(a) Ferric nitrate method. Roberson and Austin's method [26] was slightly modified for use

[19] Smith and Symons, *Trans. Faraday Soc.*, 1958, **54**, 338.
[20] Bonnemay, *J. Chim. phys.*, 1944, **41**, 18.
[21] Kelly and Smith, unpublished results.
[22] Audrieth, *Chem. Rev.*, 1934, **15**, 169.
[23] Farmer, Rigg, and Weiss, *J.*, 1955, 582.
[24] Vogel, "Text Book of Quantitative Inorganic Analysis," Longmans, Green & Co., London, 1948, p. 809.
[25] Stein and Weiss, *J.*, 1949, 3245.
[26] Roberson and Austin, *Analyt. Chem.*, 1957, **29**, 854.

with dilute azide solutions buffered at pH 8. It was found that a more concentrated ferric nitrate solution was necessary for full colour development.

To 10 ml. of ferric solution (made by dissolving 20 g. of ferric nitrate in 100 ml. of water, then adding 5 ml. of concentrated nitric acid and making up the volume to 1 l.) were added 4 ml. of 10^{-3}M-azide solution. The volume was made up to 50 ml. and the optical density, measured after 5 min., on a Unicam S.P. 600 spectrophotometer at 460 mμ using 4-cm. cells, was 0·5.

An appropriate volume of the irradiated solution was taken, so that by the above procedure, an optical density close to 0·4 was obtained. The actual optical density was then found by comparison with the standard and the result was checked by measurement against the appropriate blank.

(b) Ceric method. The oxidation of azide ion by ceric salts is the basis of two methods of estimation of azide. The first involves measurement of the nitrogen evolved and, in the second, ferrous perchlorate is titrated against excess of ceric salt solution. These methods are not wholly suitable for dilute azide solutions.

10^{-3}M-Solutions of sodium azide were found to be immediately and quantitatively oxidised by ceric sulphate in acid solution, the extent of oxidation being followed by spectrophotometric determination of the excess of ceric sulphate. The procedure was as follows: to 10 ml. of 10^{-3}M-ceric sulphate, which had been made approximately 0·8N in sulphuric acid, were added 2 ml. of concentrated sulphuric acid and 8·5 ml. of standard 10^{-3}M-buffered azide solution. After the volume had been made up to 50 ml. the excess of ceric sulphate was measured at 315 mμ in 1-cm. cells against the reference solution. An appropriate amount of the irradiated solution, treated in the same manner, was taken so that a measurable difference in optical density was obtained.

Determination of ammonia. Ammonia was determined by Beeghly's method.[27] For 10^{-3}M-azide solutions, 25—40 ml. of irradiated solution (the amount depending upon dose received) were made up to 50 ml. after addition of 1 ml. of Nessler's reagent. Measurements were made at 410 mμ in 4-cm. cells. A calibration curve was constructed by using a standard ammonium chloride solution and this was checked at regular intervals. It was necessary to make up fresh reagent each month.

The azide ion, in concentrations greater than 10^{-3}M, interfered with development of the Nessler colour. For solutions whose optical density should have been 0·2 or less, the colour was suppressed markedly; and for more concentrated ammonia solutions, the true value was reached after varying periods of time dependent upon the azide concentration, after which the optical density continued to rise.

The time elapsing before the correct optical density was reached was found for each azide concentration studied. The procedure for determination of ammonia in irradiated solutions was then as follows: Three 25 ml. samples of the irradiated solution were placed in 50 ml. flasks. To these were added severally 4, 6, and 8 ml. of standard 10^{-4}M-ammonium chloride solution, followed by 1 ml. of Nessler's reagent and water to the mark. The optical densities were then measured after the predetermined time interval. The absorption due to the added ammonia was subtracted from these values. Unless the three results thus obtained agreed to within 5%, the determination was repeated.

Determination of nitrite. Nitrite was measured after removal of azide by precipitation as silver azide. For 0·1M-azide solutions, 20 ml. of irradiated solution were added slowly with stirring to 25 ml. of 0·1M-silver nitrate which had been heated to near the b. p. The precipitate was filtered off hot (Whatman No. 542 filter-paper) and washed with 5 ml. of water. The filtrate was made up to 50 ml. when necessary. To 10 ml. of hot silver nitrate solution were added 25 ml. of filtrate, again slowly and with stirring. The filtration and washing procedure was repeated, the final volume of the filtrate being measured. Normally, this sufficed to remove all the azide present, but a confirmatory test (10 ml. of final filtrate added to 5 ml. of hot silver nitrate solution) was always carried out. Endres and Kaufman's method [28] was applied to the final filtrate and it worked excellently for standard nitrite solutions of concentrations greater than 2×10^{-6}M. For solutions of lower azide concentration, smaller amounts of silver nitrate were used and precipitation was carried out much more slowly to ensure the formation of large particles.

[27] Beeghly, *Ind. Eng. Chem. Anal.*, 1942, **14**, 137.
[28] Endres and Kaufman, *Annalen*, 1935, **518**, 109.

Determination of hydrazine and hydroxylamine. The azide ion interfered seriously with the method for hydrazine determination suggested by Pesez and Petit;[29] and Endres and Kaufman's method for determination of hydroxylamine by conversion into nitrite could not be used owing to the immediate reaction between nitrite and azide under acid conditions. The azide was therefore removed, before the determination of these products, by passing the solutions down a column of Dowex 2 (×10) (Cl form) ion-exchange resin (10 cm. × 3 cm.²). Usually 25 ml. of the solution, followed by 25 ml. of water, were passed down the column and made up to the mark in a 50 ml. flask. Treatment of these solutions with ferric nitrate showed the absence of any appreciable amounts of azide. For 0·1M- and greater concentrations of azide, each column was used once only, and was regenerated with 2N-hydrochloric acid (2 bed volumes) followed by water (10 bed volumes).

Various synthetic mixtures of hydrazine, hydroxylamine, and azide were passed through the columns. No loss of hydrazine occurred, for azide concentrations up to 1·0M, when the final concentration of hydrazine, after colour development, was in the range $2—10 \times 10^{-6}$M. Hydroxylamine, where the final concentration was in the same range, gave good results with 10^{-3}M-azide, but at the higher azide concentrations some loss occurred. As no hydroxylamine could be detected in the reactions there was no necessity to rectify this.

Detection of nitrate. Nitrate was detected, after reduction with nascent hydrogen, as nitrite.[30] The azide and any nitrite initially present were removed simultaneously by acidifying with glacial acetic acid and boiling the solution. Samples from such a treatment were added to a 25 ml. flask containing 2 ml. each of sulphanilic acid and α-naphthylamine reagents, and a trace of zinc dust. A final concentration of nitrate of 5×10^{-6}M yielded a faint but definite pink colour.

Determination of hydrogen peroxide. This was estimated with potassium iodide;[31] no interference from the azide ion up to a concentration of 1·0M was observed. The solutions were brought to pH 4·0 by the addition of sulphuric acid, before Hochanadel's reagents were added.

KING'S COLLEGE, NEWCASTLE UPON TYNE, 1. [*Received, April 13th*, 1960.]

[29] Pesez and Petit, *Bull. Soc. chim. France*, 1947, 122.
[30] Feigl, "Spot Tests," Nordemann, 1937, 202.
[31] Hochanadel, *J. Phys. Chem.*, 1952, **56**, 587.

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291. *The Radiation Chemistry of Azide Solutions. Part II.* The Action of X-Rays (200 kv) on Deærated Aqueous Solutions of Sodium Azide in the Presence of Different Organic Solutes.*

By P. KELLY and M. SMITH.

Deærated aqueous solutions of sodium azide have been irradiated with *X*-rays (200 kv) in the presence of methanol, propan-2-ol, acetone, and formaldehyde. The azide–methanol solutions have been studied over a wide range of concentrations; in all cases the main reaction products were: nitrogen, ammonia, hydrogen, ethylene glycol, and formaldehyde. The results confirm the mechanism for radiolytic decomposition of the azide ion previously presented. Studies on the azide–propan-2-ol and azide–acetone systems provide confirmatory evidence for the assumption of H_2O^- (polaron) as a primary species in the radiolysis of water.

IN the preceding paper a mechanism was presented for the action of *X*-rays (200 kv) on deærated aqueous solutions of sodium azide. Although this mechanism was able to give a coherent account of the dependence of the yields on concentration, postulation of several new reactions made it somewhat speculative. Studies of the radiolysis of aqueous solutions of methanol and propan-2-ol have confirmed the presence of the H_2O^- species (polaron, not an ionised water molecule) as one of the primary products of the

* Part I, preceding paper.

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radiolysis of water. It seemed likely, therefore, that the irradiation of sodium azide in the presence of these alcohols could provide further evidence for some of the reactions postulated.

Results.—Irradiations were carried out on solutions buffered at pH 8·0 (10^{-3}M Sörensen buffer) to avoid the presence of hydrazoic acid.

FIG. 1. *Dependence on methanol concentration of the initial yields of nitrogen* (A), *ammonia* (B), *and hydrogen* (C) *in the irradiation of deærated aqueous solutions of sodium azide* (10^{-2}M) *with* X-*rays* (200 kv).

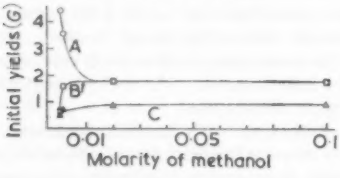


FIG. 2. *Dependence on methanol concentration of the initial yields of nitrogen* (A), *ammonia* (B) *and hydrogen* (C) *in the irradiation of deærated aqueous solutions of sodium azide* (10^{-2}M) *with* X-*rays* (200 kv).

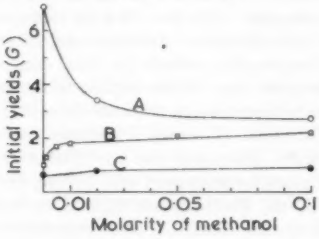


FIG. 3. *Dependence on methanol concentration of the initial yields of nitrogen* (A), *ammonia* (B), *hydrogen* (C), *and nitrous oxide* (D) *in the irradiation of deærated aqueous solutions of sodium azide* (10^{-1}M) *with* X-*rays* (200 kv).

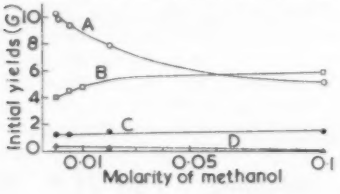


FIG. 4. *Formation of acetone by irradiation of deærated aqueous solutions of sodium azide,* (A) 5×10^{-2}M, (B) 10^{-2}M, *in the presence of propan-2-ol* (0·1M) *with* X-*rays* (200 kv).

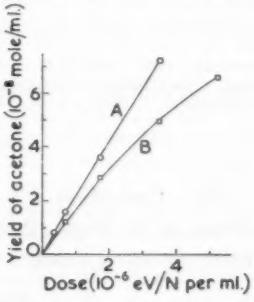


FIG. 5. *Dependence on acetone concentration of the initial yields of nitrogen in the irradiation of deærated aqueous solutions of sodium azide,* (B) 0·1M, (A) 0·5M, *with* X-*rays* (200 kv).

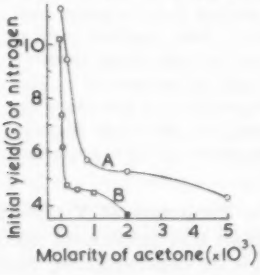
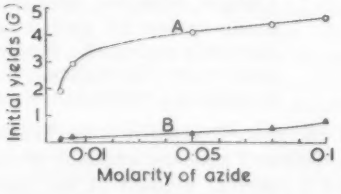


FIG. 6. *Dependence on azide concentration of the initial yields of nitrogen* (A) *and nitrous oxide* (B) *in the irradiation of deærated aqueous solutions of sodium azide in the presence of acetone* (5×10^{-4}M) *with* X-*rays* (200 kv).



Mixtures of methanol (10^{-3}—10^{-1}M) and sodium azide (10^{-3}—10^{-1}M) were irradiated with different doses. The only gaseous products were nitrogen, hydrogen, and nitrous oxide. Products tested for in solution were hydroxylamine, hydrazine, nitrite, nitrate, hydrogen

peroxide, ammonia, formaldehyde, and ethylene glycol, but only the last four of these were detected.

TABLE 1. *Dependence on the azide concentration of initial yields of products formed in the irradiation* (X-*rays*, 200 kv) *of azide solutions in the presence of methanol* (10^{-1}M *and* 10^{-3}M).

MeOH concn. (M)	Azide concn. (M)	Yields (*G* values) N_2	H_2	N_2O	NH_3	$C_2H_4(OH)_2$	CH_2O	H_2O_2
0·1	0·1	5·05	0·72	0·03	2·8	NM	2·0	0·3
0·1	0·01	2·7	0·82	NM	2·2	1·7	1·6	0·2
0·1	0·001	1·7	0·90	0·006	1·7	2·1	0·4	0·0
0·001	0·001	3·55	0·75	NM	1·6	NM	NM	NM

NM = Not measured.

TABLE 2. *Dependence on the azide concentration of initial yields of nitrogen and hydrogen in the irradiation* (X-*rays*, 200 kv) *of azide solutions in the presence of propan-2-ol* (10^{-1}M).

Azide concn. (M)	0·1	0·05	0·01
Yield of N_2	3·0	2·5	1·52
Yield of H_2	0·85	0·9	0·9

Having established the linearity of the yield–dose curves up to total doses of 6×10^{-6} ev/*N* per ml. for the gaseous products, we investigated the variation of the initial yields of

FIG. 7. *Dependence on alcohol concentration* [(A) *methanol*, (B) *propan-2-ol*] *of the initial yields of nitrogen in the irradiation of deærated aqueous solutions of sodium azide* (0·1M) *in the presence of acetone* (5×10^{-4}M) *with* X-*rays* (200 kv).

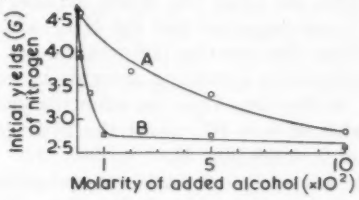
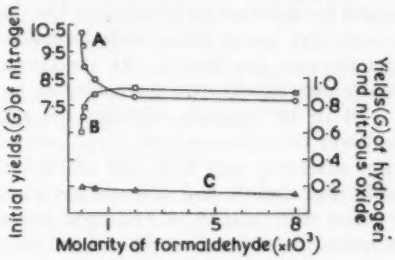


FIG. 8. *Dependence on formaldehyde concentration of the initial yields of nitrogen* (A), *hydrogen* (B), *and nitrous oxide* (C) *in the irradiation of deærated aqueous solutions of sodium azide* (0·1M) *with* X-*rays* (200 kv).



nitrogen, hydrogen, ammonia, and nitrous oxide for a variety of mixtures (Figs. 1, 2, and 3). Table 1 shows the initial yields of products for varying concentrations of azide in the presence of 0·1M-methanol, and the nitrogen, hydrogen, and ammonia yields for 10^{-3}M-azide in the presence of 10^{-3}M-methanol.

Solutions of propan-2-ol (0·1M) and sodium azide (10^{-2}—10^{-1}M) were irradiated with various doses. Analysis of the products in solution was carried out as for the methanol mixtures. The only measurable product was acetone. Ammonia was also formed but the acetone interfered so seriously with the Nessler colour as to make quantitative measurement impossible. The dose–yield curves for acetone are given in Fig. 4, and the initial yields of nitrogen and hydrogen appear in Table 2.

The effect of adding acetone before irradiation of sodium azide solutions was also studied. The initial yields of nitrogen for azide solutions (0·1—0·5M) at various acetone concentrations are given in Fig. 5. The dependence of the nitrogen yield on azide concentration at constant acetone concentration (5×10^{-4}M) (Fig. 6) and the influence of the addition of methanol or propan-2-ol on the yield of nitrogen from 0·1M-azide solutions, in the presence of acetone (5×10^{-4}M), have been studied (Fig. 7).

Fig. 8 shows the changes in the initial yields of nitrogen, hydrogen, and nitrous oxide from 0·1M-azide in the presence of varying amounts of formaldehyde.

Discussion

Azide Solutions containing Methanol.—Studies of the radiolysis of deærated aqueous methanol solutions [1] have shown that, at pH 8·0, the same values being used for the primary water decomposition yields as given in Part I, the results can be described in terms of the following reactions:

$$OH + CH_2{\cdot}OH \longrightarrow CH_2{\cdot}OH + H_2O \quad (1)$$

$$H + CH_2{\cdot}OH \longrightarrow CH_2{\cdot}OH + H_2 \quad (2)$$

$$2CH_2{\cdot}OH \longrightarrow CH_2{\cdot}OH + CH_2O \quad (3)$$

$$2CH_2{\cdot}OH \longrightarrow (CH_2{\cdot}OH)_2 \quad (4)$$

$$H_2O^- + CH_2O \longrightarrow [CH_2{\cdot}O^-] \longrightarrow CH_2{\cdot}OH \quad (5)$$

$$CH_2{\cdot}OH + H_2O_2 \longrightarrow CH_2O + OH + H_2O \quad (6)$$

$$H_2O^- + H_2O_2 \longrightarrow OH + OH^- + H_2O \quad (7)$$

$$2H_2O^- \longrightarrow H_2 + 2OH^- \quad (8)$$

The extent to which the $CH_2{\cdot}OH$ radicals distribute themselves between the dimerisation (4) and the disproportionation (3) reaction is not known exactly but appears to be such that $k_4/k_3 \sim 5$. The extent of reaction (6) as compared with (3) and (4) is also not known, but it seems probable that the maximum amount of the molecular-yield hydrogen peroxide which can be removed by this reaction is $G \sim 0{\cdot}3$.

In terms of this reaction scheme the presence of methanol in the azide solutions should result in a competition between the two solutes for the hydroxyl radicals, whilst the H_2O^- would react solely with the azide ions. Interference from the back-reaction (5) might be expected to be small at low doses, in view of the value of k_4/k_3, unless the H_2O^- reacts very much faster with formaldehyde than with the azide ion, which actually is not the case (see below). In the previous paper, it was suggested that the NH_2 radical reacts only slowly with the azide ion, so it seemed likely that reaction (16) would occur.

(i) In 10^{-3} M-azide solutions the addition of methanol in increasing amounts is seen to lower the nitrogen yield, to a limit of $G = 1{\cdot}7$. At the same time the ammonia yield rises markedly and then also reaches a limiting value of $G = 1{\cdot}7$, whilst the hydrogen yield rises slightly and then reaches a limiting value of $G = 0{\cdot}9$ (Fig. 1).

The molecular-yield hydrogen peroxide at these relatively low azide concentrations is removed *via* reaction (7) and the presence of the methanol should not alter this. The absence of hydrogen peroxide in the 0·1M-methanol solution is in agreement with this supposition.

The decrease in nitrogen yield is attributed to the methanol's removing hydroxyl radicals *via* reaction (1), thus preventing reaction (9) from occurring:

$$OH + N_3^- \longrightarrow N_3 + OH^- \quad (9)$$

The increase in the ammonia yield is thought to be due to the suppression of the back-reaction (10),

$$H_2O^- + N_2 \longrightarrow N_2^- + H_2O \quad (10)$$

this suppression being a result of (*a*) the decrease in N_3 radicals caused by the operation of reaction (1) in place of (9) and (*b*) the removal of NH_2 radicals *via* reaction (11) instead of *via* (12):

$$NH_2 + CH_2{\cdot}OH \longrightarrow NH_3 + CH_2{\cdot}OH \quad (11)$$

$$NH_2 + H_2O^- \longrightarrow NH_2^- + H_2O \quad (12)$$

The increase in hydrogen yield seems likely to be due to the operation of reaction (2),

[1] Lyon, Scholes, and Smith, unpublished results.

the limiting value of G 0·9, with allowance for the molecular-yield hydrogen $G(H_2)$ 0·6, leading to a value for $G(H)$ of 0·3.

The above suggestions lead to the following sequence for the results on the 0·1M-methanol solution:

$$H_2O^- + H_2O_2 \longrightarrow OH + OH^- + H_2O \ (G\ 0{\cdot}8) \quad (13)$$

$$H_2O^- + N_3^- \longrightarrow N_2 + NH^- + OH^- \ (G\ 1{\cdot}7) \quad (14)$$

$$NH^- + H_2O \longrightarrow NH_2 + OH^- \ (G\ 1{\cdot}7) \quad (15)$$

$$NH_2 + CH_3{\cdot}OH \longrightarrow NH_3 + CH_2{\cdot}OH \ (G\ 1{\cdot}7) \quad (16)$$

$$H + CH_3{\cdot}OH \longrightarrow H_2 + CH_2{\cdot}OH \ (G\ 0{\cdot}3) \quad (17)$$

$$OH + CH_3{\cdot}OH \longrightarrow CH_2{\cdot}OH + H_2O \ [G\ 3{\cdot}2 = G(OH)\ 2{\cdot}4 + G(OH)\ 0{\cdot}8 \text{ from } (13)] \quad (18)$$

This sequence clearly leads to an explanation of the results in terms of the primary water yields. Also, on the basis of this sequence, the $CH_2{\cdot}OH$ radical yield should be:

$$G(CH_2{\cdot}OH) = 3{\cdot}2\ (18) + 1{\cdot}7\ (16) + 0{\cdot}3\ (17) = 5{\cdot}2$$

(The numbers in parentheses represent the reactions responsible for $CH_2{\cdot}OH$ radical production.) The expected total yield for the aldehyde and glycol is thus $G = 2{\cdot}6$, which is confirmed by the experimental values of G(glycol) = 2·1, and G(formaldehyde) = 0·4. (These values are also in good agreement with the value of 5 for k_4/k_3.)

At equal concentrations of methanol and azide (10^{-3}M), $G(N_2) = 3{\cdot}55$, $G(NH_3) = 1{\cdot}6$, and $G(H_2) = 0{\cdot}75$. The decrease in ammonia and hydrogen yields as compared with those in the 0·1M-methanol solution represents a loss of G 0·25 [G(H) 0·15 plus $G(H_2O^-)$ 0·1]. In terms of the above reactions this deficiency must result from the operation of the back-reaction (10), which is enhanced by the increased extent of reaction (9) as compared with (1). The yield of nitrogen from reaction (9) is G 1·95 [$G(N_2)$ 3·55 − $G(N_2)$ 1·6 from (14)] so that, after allowance for the back-reaction (G 0·25), the extent of reaction (9) must be G 1·55. The total hydroxyl radical yield is $G = 3{\cdot}2$, *i.e.*, 2·4 from G(OH) plus 0·8 from reaction (13). As G 1·55 of this must participate in reaction (9), G 1·65 is reacting with the methanol (1), and consequently the ratio of the rate constants

$$k_{OH + N_3^-}/k_{OH + CH_3{\cdot}OH} = k_9/k_{18} = 1{\cdot}55/1{\cdot}65 \sim 0{\cdot}94.$$

The hydrogen yield, which is increased in the presence of methanol, does not appreciably change when the methanol concentration is increased from 10^{-2} to 10^{-1}M. This suggests that all the available hydrogen atoms are reacting with methanol. This limit of hydrogen is $G(H_2) = 0{\cdot}9$; thus with a molecular yield of 0·6, a value for G(H) = 0·3 is obtained.

(ii) In 10^{-2}M-azide solutions the addition of methanol also results in a decrease in the nitrogen yield and an increase in the ammonia and hydrogen yields. At 0·1M-methanol the ammonia yield is increased to $G(NH_3) = 2{\cdot}2$, and that this is due to a release of H_2O^- from reaction (13) is confirmed by the appearance of hydrogen peroxide as a product.

The yield of nitrogen [$G(N_2) = 2{\cdot}7$] is slightly greater than that of the ammonia, and if the excess is taken as a result of reaction (9), a value for $k_9/k_{18} \sim 0{\cdot}93$ is obtained, which agrees well with the value calculated above, although some uncertainty could be involved in using the relatively small difference in the nitrogen yields. This excess represents a value of 0·3 for G(OH) consumed in (9), leaving G(OH) = 2·1 to react *via* (18).

The $CH_2{\cdot}OH$ radical yield at 10^{-1}M-methanol should be:

$$\begin{aligned} G(CH_2{\cdot}OH) &= 2{\cdot}2 \text{ [from } NH_2 + CH_3{\cdot}OH \text{ (16) as the ammonia yield is 2·2]} \\ &\quad + 0{\cdot}2 \text{ [from H + } CH_3{\cdot}OH \text{ (17) as the hydrogen yield is 0·82]} \\ &\quad + 0{\cdot}6 \text{ [from the OH radicals produced from molecular-yield hydrogen peroxide } \textit{via} \text{ (6) and (7) as } G(H_2O_2) \text{ is only 0·2]} \\ &\quad + 2{\cdot}1 \text{ [from } G\text{(OH) (18) minus those OH radicals consumed in (9)]} \\ &= 5{\cdot}1 \end{aligned}$$

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The aldehyde and glycol yields should thus be similar to those found in 10^{-3}M-azide solutions. The experimental values were G(glycol) = 1·7 and G(aldehyde) = 1·6. It is thought that this high aldehyde yield could be due to the presence of some heavy-metal impurities which might react with the CH_2·OH radicals according to:

$$M^{(n+1)+} + CH_2{\cdot}OH \longrightarrow M^{n+} + CH_2O + H^+ \quad . . . . . (19)$$

Some support for this comes from experiments on 10^{-3}M-azide solutions in the presence of 0·1M-methanol where the prior addition of 10^{-6}M-ferric nitrate resulted in a doubling of the aldehyde yield. The source of these impurities is most likely to be sodium azide.

(iii) In 0·1M-azide solutions, in the presence of 0·1M-methanol, the ammonia yield is $G(NH_3) = 2·8$, and if this ammonia is produced by reaction of the NH_2 radicals with methanol by reaction (16), then, of the yield of $G(N_2) = 5·05$, the proportion $G(N_2) = 2·25$ is to be ascribed to reaction (9). This assignment is supported by the fact that it leads to a value for $k_9/k_{18} = 1·0$. The total hydroxyl radical yield required to obtain such a ratio was taken as G(OH) = 2·9. This value is the sum of the primary hydroxyl radical yield, G(OH) = 2·4 and $G = 0·5$ hydroxyl radicals formed from the decomposition of molecular-yield hydrogen peroxide by reaction (6) and, because a small yield of nitrous oxide is obtained by reaction (20):

$$N_3 + H_2O_2 \longrightarrow N_2 + NOH + OH \quad . . . . . (20)$$

The expected CH_2·OH radical yield was:

$$G(CH_2{\cdot}OH) = 2·8\ (16) + 0·5\ [(6) \text{ and } (20) \text{ followed by } (18)] + 0·9\ [(18) - (9)]$$
$$= 4·2$$

The aldehyde yield was in fact $G = 2·0$, but no value for the glycol yield could be obtained because of the difficulties of estimating glycol in the presence of a high concentration of sodium azide. The aldehyde yield is in keeping with the supposition that the heavy-metal ion impurities come from the sodium azide used.

The decrease in the nitrogen yield, when the methanol concentration is increased, is too great to be explained in terms of a value of $k_9/k_{18} = 1·0$. However, if the NH_2 radical reacts with the azide ion according to (21), then the added methanol should decrease the nitrogen yield produced by reaction (21) as well as (9). On this basis the decrease in nitrogen is well accounted for.

$$NH_2 + N_3^- \longrightarrow N_3 + NH_2^- \quad . . . . . (21)$$

Azide Solutions in the Presence of Propan-2-ol.—Irradiation with γ-rays (^{60}Co) of deærated aqueous solutions of propan-2-ol leads to the formation of acetone and hydrogen.[2] At pH 8·0 the yields of both these products are $G \sim 1·0$. The following reaction sequence can account for this result:

$$OH + CHMe_2{\cdot}OH \longrightarrow CMe_2{\cdot}OH + H_2O \quad . . . . . (22)$$
$$H + CHMe_2{\cdot}OH \longrightarrow CMe_2{\cdot}OH + H_2 \quad . . . . . (23)$$
$$2CMe_2{\cdot}OH \longrightarrow COMe_2 + CHMe_2{\cdot}OH \quad . . . . . (24)$$
$$H_2O^- + COMe_2 \longrightarrow [COMe_2]^- \longrightarrow CMe_2{\cdot}OH + H_2O \quad . . . . . (25)$$
$$H_2O^- + H_2O_2 \longrightarrow OH + OH^- + H_2O \quad . . . . . (26)$$
$$CMe_2{\cdot}OH + H_2O_2 \longrightarrow COMe_2 + OH + H_2O \quad . . . . . (27)$$

The irradiation of solutions of azide containing propan-2-ol is seen to lead to a very large increase in the yield of acetone. This is expected in terms of reaction (14) which will

[2] Allan and Scholes, *Nature*, 1960, **187**, 218.

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decrease the back-reaction (25) and at the same time increase the radical yield according to:

$$NH_2 + CHMe_2{\cdot}OH \longrightarrow CMe_2{\cdot}OH + NH_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (28)$$

In 10^{-2}M-azide solutions in the presence of 0·1M-propan-2-ol there is a marked curvature in the yield–dose curve for acetone, and this suggests that H_2O^- reacts very much faster with acetone than with the azide ion. That this curvature is a result of reaction (25) is confirmed by the rather more nearly linear yield–dose curve obtained in 5×10^{-2}M-azide solutions. These curves both give a ratio for the rate constant ratio $k_{25}/k_{14} \sim 10^3$.

In 0·1M-azide solutions in the presence of 0·1M-propan-2-ol the yield of nitrogen $G(N_2) = 3{\cdot}0$ is less than that obtained from the corresponding solution containing methanol; hence the hydroxyl radicals must react faster with propan-2-ol than with methanol. In 10^{-2}M-azide solutions in the presence of 0·1M-propan-2-ol the hydrogen yield was $G(H_2) = 0{\cdot}9$, which gives a value of $G(H)$ 0·3, the same as with methanol.

Azide Solutions in the Presence of Acetone.—The ratio of the rate constants $k_{25}/k_{14} \sim 10^3$, deduced from the above experiments, suggested that the addition of increasing amounts of acetone to a 0·1M-azide solution would result in a decrease in the nitrogen yield to a limiting value corresponding to $\{G(OH) + G(H)\}$ plus the yield of nitrogen resulting from hydrogen peroxide consumption in reactions (27) and (20). The nitrogen does indeed fall sharply to a limiting value, but at higher acetone concentrations a further decrease in the nitrogen yields occurs. The " plateau region " in which the nitrogen yield remains constant (see Fig. 5) has a value $G(N_2) = 4{\cdot}65$, reasonably close to the calculated figure $G(N_2) = 5{\cdot}5$. The onset of the " plateau region " corresponds to a value for the rate constant ratio $k_{25}/k_{14} \sim 2 \times 10^3$. Increasing the concentration to 0·5M-azide results in a five-fold increase in the amount of acetone required to reach this region, confirming the existence of a competition between acetone and azide for H_2O^-. The nitrogen yield $G(N_2) = 5{\cdot}3$ in the " plateau region " in 0·5M-azide solutions is closer to the expected value and again falls off at high acetone concentrations.

The decrease in the nitrogen yield, below the " plateau region " value, suggests that the acetone interacts with the hydroxyl radicals. This is supported by the marked decrease of the nitrogen yield which occurs when the azide concentration is lowered at constant acetone concentration (5×10^{-4}M) (Fig. 6).

A possible mechanism is the abstraction of a hydrogen atom from the acetone; the influence of the acetone upon the nitrogen yield is so large as to make the rate of this reaction faster than that between methanol and the hydroxyl radical, a result in strong contrast to the results of Merz and Waters.[3]

As nearly all the nitrogen in the " plateau region " will come from the recombination of N_3 radicals, the nitrous oxide yield would be expected to be quite high. The experimental figure for $G(N_2O) = 0{\cdot}17$ is to be compared with the nitrous oxide yield from 0·1M-azide in the presence of 0·1M-methanol where $G(N_2) = 5{\cdot}05$ but $G(N_2O) = 0{\cdot}03$. In view of the results obtained in the radiolysis of the alcohol–azide solutions, the addition of methanol and propan-2-ol in the " plateau region " should result in a decrease of the nitrogen yield, this decrease being governed by the appropriate rate constant ratio (*e.g.*, for methanol by k_9/k_{18}). Somewhat surprisingly, the nitrogen yields tend to a limiting value of *ca.* $G(N_2) = 2{\cdot}0$ for both methanol and propan-2-ol (Fig. 7).

Azide Solutions in the Presence of Formaldehyde.—Formaldehyde has been found to react with H_2O^-, so it seemed likely that the addition of formaldehyde to azide solutions would produce a similar pattern of results to those found with acetone. A sharp decrease in the nitrogen yield does occur, but the limiting value $G(N_2) = 7{\cdot}5$, is far too high to correspond to removal of H_2O^- (Fig. 8). As the nitrogen yield decreases, that of hydrogen increases, and also reaches a limiting value which corresponds to a $G(H)$ 0·3. The formaldehyde thus reacts very much faster with hydrogen atoms than does methanol, a result

[3] Merz and Waters, *J.*, 1949, S13.

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in keeping with other experiments.[4] Therefore, it seems likely that the NH_2 radicals also react rapidly with formaldehyde. The fall in the yield of nitrogen from $G(N_2) = 10{\cdot}2$ to 7·5 could be a result of the removal of NH_2 radicals from reaction (21). If this explanation is correct, then no reaction between H_2O^- and formaldehyde has occurred, so this reaction must be very much less effective than that between acetone and H_2O^-.

Experimental

The experimental procedures were the same as those described in the preceding paper, apart from the following additions.

Evacuation and Collection of Gaseous Products.—The loss of acetone which occurred during evacuation of azide–acetone mixtures was found by estimation of the acetone content before and after evacuation. This loss depended on the acetone concentration and was *ca.* 5—15% for the concentration range 8×10^{-5}—2×10^{-3}M-acetone. The gaseous products were collected over solid carbon dioxide–acetone traps as it was found that nitrogen was retained to a small but significant extent by liquid air. To avoid too much contamination of the gaseous products these traps were cleaned after each collection.

Gas Analysis.—The presence of methanol, from 5 to 10 moles % in the gas samples, resulted in a slightly greater uncertainty in the nitrogen and nitrous oxide content, due to contributions to *m/e* 32 (air peak) and *m/e* 30 (reference peak for nitrous oxide) from the methanol. In the propan-2-ol experiments, samples were contaminated by acetone (~3·0), propan-2-ol (~0·4), propene (~3·5), and methane (~1·5 moles %). However, there was no serious interference with the determination of hydrogen, nitrogen, and nitrous oxide.

Analysis of Solutions.—Ammonia. In methanol–azide mixtures, ammonia was determined by the method described in Part I, unirradiated mixtures of methanol, azide, and standard ammonium chloride solution being used to establish the time at which the correct optical density was reached.

Acetone. Irradiated azide–propan-2-ol mixtures were analysed for acetone by the salicylaldehyde method.[5] The presence of sodium azide did not interfere with the determination.

Ethylene glycol. The glycol content of irradiated mixtures of azide and methanol was determined, after the removal of azide, by a modification [1] of Aspinall and Ferrier's method.[6] The azide was removed by acidification with sulphuric acid, followed by boiling. Experiments with standard glycol solutions showed that no loss of glycol was incurred by this procedure.

Formaldehyde. Formaldehyde was determined by a modification [1] of Johnson and Scholes's method.[7] The azide ion did not interfere.

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King's College, Newcastle upon Tyne, 1. [*Received, April 13th,* 1960.]

[4] Steacie, "Atomic and Free Radical Reactions," Reinhold Publ. Corp., 1954, p. 594.
[5] Berntsson, *Analyt. Chem.*, 1956, **28**, 1337.
[6] Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1216.
[7] Johnson and Scholes, *Analyst*, 1954, **79**, 217.

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292. *The Reactions of Carbene with Alkyl Halides.*

By J. N. Bradley and A. Ledwith.

Carbene (methylene) has been allowed to react with mixtures of simple alkyl halides. The major products were formed by attack at the C–Cl and the α-C–H bonds, the order of reactivity for the C–Cl bond being primary > secondary > tertiary. The nature of the various products has been interpreted on the basis of the formation of a bicyclic intermediate.

The reactions of carbenes with a wide range of organic compounds have now been investigated [1] and it has been established that carbene and its derivatives behave as electrophilic reagents.[2] Carbene (methylene) itself shows very little discrimination between the various types of C–H and C=C bonds [3] although recent evidence [4] shows a small but definite trend of the form, tertiary > secondary > primary, in its reactions with simple C–H bonds.

Franzen [5] has shown that carbene reacts with both C–Cl and C–H bonds in simple alkyl halides, the reactivity towards the former being, on the average, about ten times greater. The present investigation was conducted in order to determine whether the C–Cl bonds in a series of halides show the same order of reactivity as the C–H bonds in the simple paraffins.

Experimental

Diazomethane was prepared from *N*-nitrosomethylurethane by Bawn and Rhodes's method,[6] and the vapour was passed, in a stream of dry nitrogen, into the alkyl halide mixture at −20°. The carbene was generated by photolysing this mixture with a Hanovia 500-w mercury-vapour lamp in a quartz vessel at 15°, no attempt being made to select a precise wavelength. The products were analysed by vapour-chromatography through an 11 ft. squalane column at 68° or at 90°. The alkyl halides were supplied by B.D.H. Ltd. and were fractionated before use. The purity of each halide was checked by vapour-phase chromatography.

The amount of each product formed was determined by measuring the area under the respective peak on the chromatogram. As only low conversions were obtained, it was necessary to operate the instrument at maximum sensitivity. This caused the reactant peaks to run off the scale so that only the relative peak areas corresponding to the various products could be obtained with any degree of accuracy. The results of the critical experiments are shown in Table 1, where, of the many experiments performed, only those with the largest peak areas, and hence the greatest accuracy, are included. To obtain the average ratios of the final column, the results have been weighted to favour the most accurate experiments.

The possible errors quoted here are based on the deviation between different experiments and on the accuracy with which peaks could be measured on the chromatograph traces. The n-propyl chloride was found to be contaminated with small amounts of isopropyl chloride and either s-butyl or isobutyl chloride. As further purification proved to be impracticable, allowance was made for these halides in the analysis. By virtue of the nature of the products formed, such impurities will only be important in the experiments on n-propyl–isopropyl chloride mixtures, in which the latter halide yields products similar to the contaminants. For this reason, the result of only one significant experiment is reported for this mixture and, as it is difficult to assess the error likely to be introduced, no reliance has been placed on the ratio obtained when determining the sequence of reactivities. The only other consideration used in weighting the data has been to assume that ratios given directly in a single experiment are

[1] Trotman-Dickenson, *Ann. Reports*, 1958, **55**, 47; Hine and van der Veen, *J. Amer. Chem. Soc.*, 1959, **81**, 6446.
[2] Skell and Garner, *J. Amer. Chem. Soc.*, 1956, **78**, 5430; Doering and Henderson, *ibid.*, 1958, **80**, 5274; Ledwith and Bell, *Chem. and Ind.*, 1959, 459.
[3] Knox, Trotman-Dickenson, and Wells, *J.*, 1958, 2897; Doering, Buttery, Laughlin, and Chaudhuri, *J. Amer. Chem. Soc.*, 1956, **78**, 3224; Butler and Kistiakowsky, *ibid.*, 1960, **82**, 764.
[4] Frey, *J. Amer. Chem. Soc.*, 1958, **80**, 5005; Doering and Knox, *ibid.*, 1956, **78**, 4947.
[5] Franzen, *Annalen*, 1959, **627**, 22.
[6] Bawn and Rhodes, *Trans. Faraday Soc.*, 1954, **50**, 934.

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TABLE 1. *Experimental results: reactions of* CH_2 *radicals with alkyl halides.*

Reactants	Products	Areas from chromatograph records (cm.²) I	II	III	IV	Mean ratio (*a*)/(*b*)
Pr^nCl	Bu^nCl (*a*)	0·54	0·12			2·0 ± 0·2
Bu^tCl	$Bu^t{\cdot}CH_2Cl$, $Bu^n{\cdot}CH_2Cl$ (*b*)	0·27	0·06			
Pr^nCl	Bu^nCl (*a*)	0·33				2·1 ± 0·1
Pr^iCl	Bu^iCl, Bu^sCl (*b*)	0·15				
Pr^iCl	Bu^iCl, Bu^sCl (*a*)	0·50	0·39			1·5 ± 0·1
Bu^tCl	$Bu^t{\cdot}CH_2Cl$, $Bu^s{\cdot}CH_2Cl$ (*b*)	0·37	0·25			
Pr^iCl	Bu^iCl, Bu^sCl (*a*)	0·24	0·20	0·16	0·16	1·0 { −0·1 +0·05
Bu^nCl	$Bu^n{\cdot}CH_2Cl$ (*b*)	0·23	0·21	0·19	0·17	
Bu^iCl	$Bu^i{\cdot}CH_2Cl$ (*a*)	0·38	0·27			1·4 ± 0·2
	$Pr^i{\cdot}CHMeCl$	0·33	0·24			
Bu^tCl	$Bu^t{\cdot}CH_2Cl$, Pr^iCMe_2Cl (*b*)	0·24	0·22			
Bu^iCl	$Bu^i{\cdot}CH_2Cl$ (*a*)	0·18	0·09			0·45 ± 0·05
	$Pr^i{\cdot}CHMeCl$	0·17	0·09			
$(CH_2Cl)_2$	$CH_2(CH_2Cl)_2$ (*b*)	0·41	0·19			
Bu^sCl	$Bu^s{\cdot}CH_2Cl$ (*a*)	0·07	0·05			0·45 ± 0·10
Bu^tCl	$Bu^t{\cdot}CH_2Cl$, $CEtMe_2Cl$	0·15	0·14			
Bu^sCl	$Bu^s{\cdot}CH_2Cl$ (*a*)	0·79	0·36			1·45 ± 0·05
	$CEtMe_2Cl$ (*b*)	0·57	0·24			

more reliable than those obtained indirectly by comparing the results from two different mixtures containing a common component.

The ratio of reactivities of t-butyl chloride and s-butyl chloride assumes some importance in the subsequent discussion. The experiments conducted with this mixture were repeated with halides from different sources and, in each case, the t-butyl chloride was found to be significantly the more reactive.

RESULTS AND DISCUSSION

The first series of experiments was carried out to characterise the products from the individual halides. In all cases, the major product was due to the insertion of CH_2 at the C–Cl bond. Some reaction also occurred at the C–H bonds, the extent depending critically on the nature of the halide; with each halide, the α-hydrogen position was predominantly attacked. The results are summarised in Table 2. Small quantities of degraded products were also observed; some of these appeared to be halides of lower molecular weight, others contained olefinic bonds and were probably unsaturated halides or simple olefins.

In order to determine the relative rates of attack of CH_2 radicals at the C–Cl bonds in different alkyl halides, a second series of experiments employed pairs of alkyl halides in equimolecular amounts. Because of the low conversions (2—5%), the products were frequently swamped in the chromatograms by the unchanged halides. This prevented many of the more interesting combinations from being studied and considerably reduced the accuracy of analysis. As pure samples of several of the higher halides were not available, it was also necessary to assume that the detector unit possessed a similar sensitivity to all species. This approximation was found to be satisfactory in all examples in which it could be checked. By combining data from different pairs of reactants and correcting them for the formation of inseparable products from isopropyl chloride and t-butyl chloride by means of Franzen's data,[5] the following sequence for the order of reactivity at the C–Cl bond was compiled: Pr^nCl 3·5; $(CH_2Cl)_2$ * 3·2; Bu^iCl 2·3; Bu^nCl 2·2; Pr^iCl 1·5; Bu^tCl 1·0; Bu^sCl 0·8.

A mechanism for the reaction must take into account the following observations: The reactivity towards a series of isomers decreases in the order, primary > secondary > tertiary. s-Butyl chloride is anomalous, being less reactive than t-butyl chloride. Attack at the C–H bonds takes place preferentially at the α-position. The extent of C–H attack

TABLE 2. *Major products from the reaction of* CH_2 *radicals with alkyl halides.*

Reactant	Products: C–Cl attack	Products: α-C–H attack
$CH_3{\cdot}CH_2{\cdot}CH_2Cl$ *	$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Cl$	$CH_3{\cdot}CH_2{\cdot}CHCl(CH_3)$
$(CH_3)_2CHCl$ *	$(CH_3)_2CH{\cdot}CH_2Cl$	$(CH_3)_2C(CH_3)Cl$
$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Cl$	$CH_3{\cdot}[CH_2]_4{\cdot}Cl$ (>90%)	$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CHCl(CH_3)$ (<10%)
$CH_3{\cdot}CH_2{\cdot}CHCl(CH_3)$	$CH_3{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2Cl$ (59%)	$CH_3{\cdot}CH_2{\cdot}C(CH_3)_2Cl$ (41%)
$(CH_3)_2CH{\cdot}CH_2Cl$	$(CH_3)_2CH{\cdot}CH_2{\cdot}CH_2Cl$ (53%)	$(CH_3)_2CH{\cdot}CH(CH_3)Cl$ (47%)
$(CH_3)_3CCl$	$(CH_3)_3C{\cdot}CH_2Cl$	—

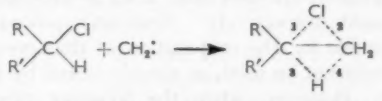
* The amounts of α-C–H attack on n- and iso-propyl chloride could not be measured with sufficient accuracy. However, there was no doubt that the quantities of such products were lower than from C–Cl attack.

varies markedly over the range of isomers, independently of the reactivity of the C–Cl bond.

The sequence of reactivity of the C–Cl bond demonstrates that an ionic intermediate, such as might involve intermediate carbonium-ion formation, can be eliminated. As CH_2 undergoes many reactions which are most satisfactorily explained by a two-pronged attack leading to a cyclic intermediate, *e.g.*, addition to a C=C double bond to give a cyclopropane, it appears likely that simple three-membered rings may be the initial products, *e.g.*:

Whilst these two types of intermediate account satisfactorily for the nature of the products, they provide no direct explanation of the four characteristic properties listed above, or of the appearance of small quantities of unsaturated products, and it is evident that, although these intermediates may appear at some stage during the process, the actual mechanism must be somewhat more complex. One way in which this difficulty can be resolved is suggested below.

In all the alkyl halides studied here, except for t-butyl chloride, a hydrogen atom is attached to the α-carbon atom and a bicyclic intermediate of the type:



may be postulated. Such an intermediate, which might also be considered as representing a form of neighbouring group-interaction,[7] can break down to form a stable molecule in

* Corrected for the presence of two C–Cl bonds.

[7] Winstein, *Bull. Soc. chim. France*, 1951, **18**, 55; Winstein and Takahoshi, *Tetrahedron*, 1958, **2**, 316.

two ways: either by rupture of bonds 1 and 4, to give the same product as insertion at the C–Cl bond, or by rupture of bonds 2 and 3, which is equivalent to attack at the α-hydrogen position. The formation of a bicyclic intermediate would be enhanced by additional hydrogen at the first carbon atom, so that the reactivity order, primary > secondary > tertiary, would be expected. In computing reactivities of C–Cl bonds, it then becomes necessary to include the products of α-hydrogen attack. The effect of this on the order of reactivity above is to move s-butyl chloride from its anomalous position on the right of the t-butyl compound, without affecting the relative positions of the other halides. The bicyclic intermediate naturally explains why attack at the α-position is favoured, the relative amounts of C–Cl and α-C–H reaction presumably being related to the effect of α-carbon substituents.

Similar bicyclic intermediates have been proposed to explain the mutarotation solvolysis of cholest-5-ene dibromide in non-polar media.[8] Moreover, the formation of small amounts of unsaturated products, observed in the present experiments, can be readily explained by the elimination of hydrogen chloride from the bicyclic intermediate, bonds 1—4 all breaking during the process.

The reactivity sequence for the C–Cl bond could also be explained on the basis of increased nucleophilic character caused by isovalent hyperconjugation,[9] but this would not account for the preferred reaction at the α-C–H rather than at the β-C–H position, although such an explanation might be valid for the reactions of carbene at C–H bonds in simple paraffins.[4]

Attempts to obtain corresponding information for the alkyl bromides have so far been unsuccessful, though preliminary results indicate that isopropyl bromide has a reactivity about twice that of isopropyl chloride.

Department of Inorganic and Physical Chemistry,
University of Liverpool. [*Received, July 21st,* 1960.]

[8] Grob and Winstein, *Helv. Chim. Acta*, 1952, **35**, 782; Winstein and Robinson, *J. Amer. Chem. Soc.*, 1958, **80**, 178.
[9] Mulliken, *Tetrahedron*, 1959, **5**, 253.

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293. *Alicyclic Studies. Part XV.* Preparation and Reactions of 3,3′-Bi-indenyl and 2,3:2′,3′-Dibenzobi(cyclohepta-2,7-dienyl).*

By Yanina Altman and David Ginsburg.

3,3′-Bi-indenyl and 2,3:2′,3′-dibenzobi(cyclohepta-2,7-dienyl) have been prepared and their behaviour in Diels–Alder reactions has been investigated.

An improved preparation and Diels–Alder reactions of bi(cyclopent-1-enyl) and bi(cyclohept-1-enyl) have been described.[1] This study reports the extension to the corresponding benzo-fused derivatives.

Reduction of indan-1-one and benzocyclohepten-3-one by the method of Barnett and Lawrence[2] gave 1,1′-bi-indanyl-1,1′-diol and 2,3:2′,3′-dibenzobi(cyclopent-3-enyl)-1,1′-diol, in 25% and 10% yield, respectively. Newman's procedure for the reduction of tetralones[3] was found suitable for the preparation of the seven-membered diene in one step in 75% yield but it could not be used, as already noted by Bell and Waring,[4] for the reduction of indan-1-one. However, when the Newman procedure was modified by

* Part XIV, Altman and Ginsburg, *J.*, 1959, 466.
[1] Part XIII, Greidinger and Ginsburg, *J. Org. Chem.*, 1957, **22**, 1406.
[2] Barnett and Lawrence, *J.*, 1935, 1104.
[3] Newman, *J. Amer. Chem. Soc.*, 1940, **62**, 1683.
[4] Bell and Waring, *J.*, 1949, 2689.

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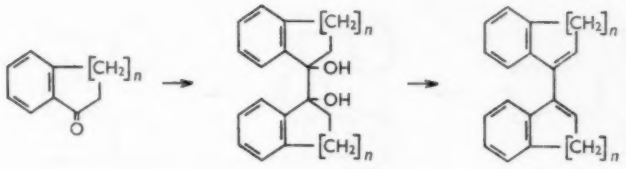
decomposition of the excess of aluminium with Rochelle salt under neutral conditions, the corresponding five-membered pinacol (I; $n = 1$) and diene (II; $n = 1$) were obtained in 70% overall yield. [The formulæ for the substances (II) are written in the *cisoid* form as they react in the Diels–Alder reaction. Presumably the *transoid* form is more stable with less steric interference of hydrogen atoms.]



(I) (II)

Dehydration of the pinacol was effected with a mixture of acetic acid and acetic anhydride. The resulting diene (II; $n = 1$) has already been prepared by another route, the yield being first reported [5] to be 48% but later 8%.[6]

Diels–Alder reactions were carried out between the two dienes (II; $n = 1$ and 3) and maleic anhydride, dimethyl acetylenedicarboxylate, and benzoquinone. In contradistinction to our experience with bi(cyclopent-1-enyl) and bi(cyclohept-1-enyl) which reacted exothermically with maleic anhydride, the benzo-fused dienes, as expected, required an excess of dienophile and heating for 3 hr.

The seven-membered adduct (VIII) was aromatised by lead tetra-acetate,[3] but the five-membered adduct (III) withstood these conditions as well as attempted aromatisation by *N*-bromosuccinimide. 5,8-Dihydroindeno[2,1-*c*]fluorene (IV) was obtained, as already reported,[6] by long heating with palladised carbon or by pyrolysis of (III) in the presence of copper powder. Oxidation afforded the hitherto unknown 5,8-dihydro-5,8-dioxoindeno[2,1-*c*]fluorene (V).

The corresponding seven-membered hydrocarbon (IX) was obtained by oxidative decarboxylation [7] with lead dioxide.

Differences in behaviour between the five- and the seven-membered homologues were found also in the reactions with dimethyl acetylenedicarboxylate: (II; $n = 3$) afforded an adduct; the former (II; $n = 1$) surprisingly did not react.

The diene reaction with benzoquinone was carried out by the procedure described by Davies and Porter.[8] Acetic acid as solvent prevents the formation of phenolic products and permits effective separation of quinhydrone from the products. Here, also, the compounds (II; $n = 1$ and 3) behaved differently. The latter ($n = 3$) afforded the tetrahydronaphthaquinone (XIII) or the more highly oxidised compound (XIV) depending on reaction conditions. The compound (II; $n = 1$) reacted much more rapidly and afforded the product formulated as (VI) or the bis-adduct (VII), depending on experimental conditions. The compound (XIII) was readily converted into the dihydric phenol (XV; R = H) or into the diacetate (XV; R = Ac).

Ultraviolet Spectra.—The spectrum of the hydrocarbon (IV) is similar to that of fluorene, except that it contains more fine structure. On the other hand, the spectrum of the analogue (IX) shows three high-intensity maxima in the 220—270 mμ range, lacking the fine structure shown by (IV). The spectrum of compound (IX) shows a striking resemblance to that of 1,2,7,8-tetrahydro-3,4:5,6-dibenzophenanthrene. The absence of coplanarity in the last two compounds as opposed to the apparent planarity of the

[5] Straus, Kühnel, and Haensel, *Ber.*, 1933, **66**, 1847.
[6] Deuschel, *Helv. Chim. Acta*, 1952, **35**, 1774.
[7] Doering, Farber, and Sayigh, *J. Amer. Chem. Soc.*, 1952, **74**, 4370.
[8] Davies and Porter, *J.*, 1957, 4958, 4961, 4967.

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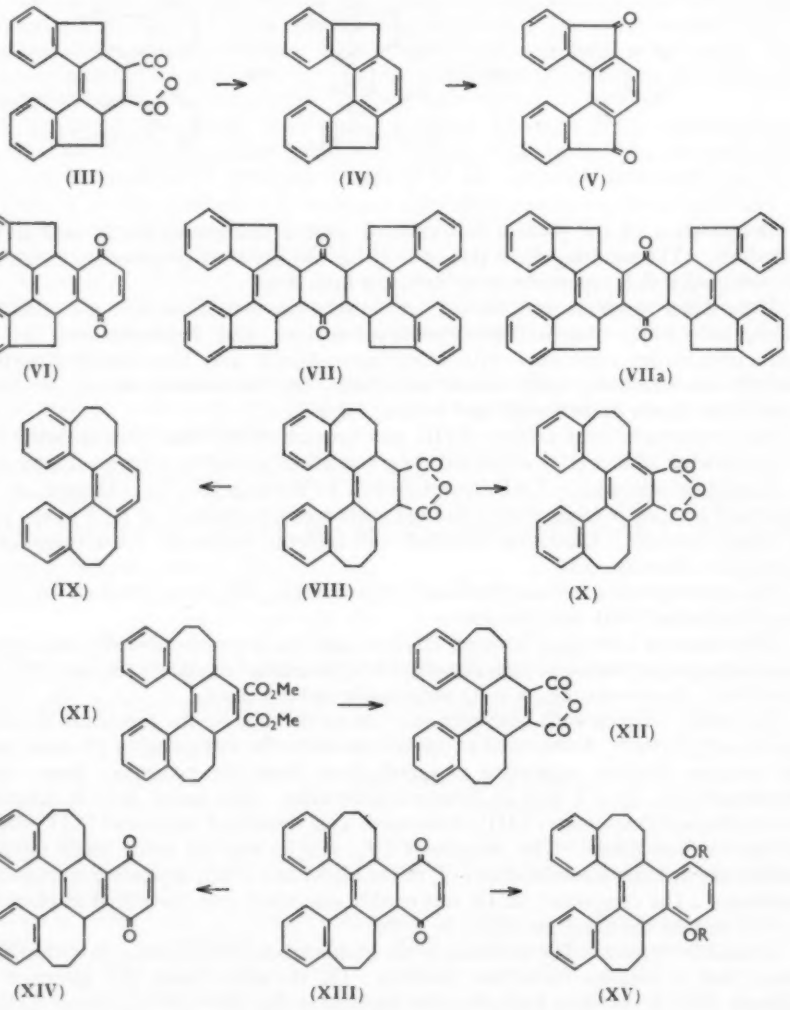
" fluorene " (IV) (this may also be seen in models) may account for the disappearance of the fine structure in the non-planar compounds (see Fig. 1).

The spectrum of the adduct (VI) clearly shows the typical absorption [9] of a *p*-quinone chromophore ($\lambda_{max.}$ 257; log ε 4·46) and of the *cis*-stilbene [10] ($\lambda_{max.}$ 295; log ε 4·43) at longer wavelength and with higher intensity. The spectrum of the seven-membered



homologue (XIV), however, retains only the quinone absorption (*ca.* 250 mμ) with reduced intensity. The *cis*-stilbene absorption appears only as an inflexion at about 300 mμ with greatly reduced intensity (log ε 3·14). This is regarded as further proof of coplanarity (or its absence) in the pentacyclic systems under discussion (see Fig. 2).

[9] Braude, *J.*, 1945, 492.
[10] Beale and Roe, *J.*, 1953, 2755.

The typical *cis*-stilbene absorption is also shown in the spectrum of the bis-adduct (VII). The absence of any absorption maximum in the 250 mμ region indicates the

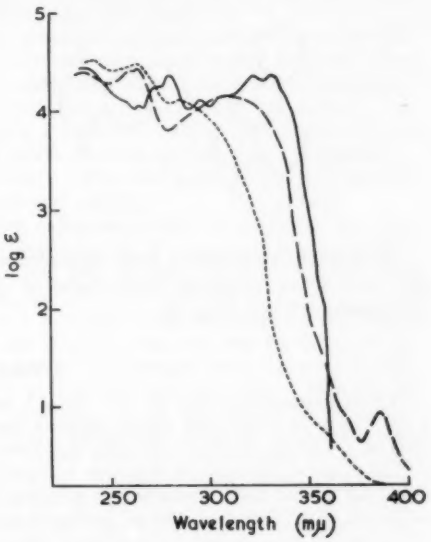


FIG. 1. (IV) (——) *in methylcyclohexane.* (IX) (. . . .) *in methylcyclohexane.* 1,2,7,8-*Tetrahydro*-3,4:5,6-*dibenzophenanthrene* (– – – –) (cf. Part XIV).

FIG. 2. (VI) (. . . .), (VII) (– – – –), *and* (XIV) (——), *in dioxan.*

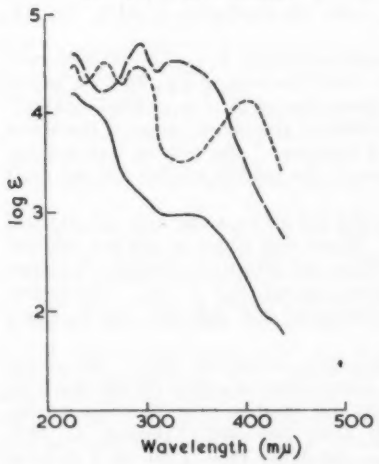
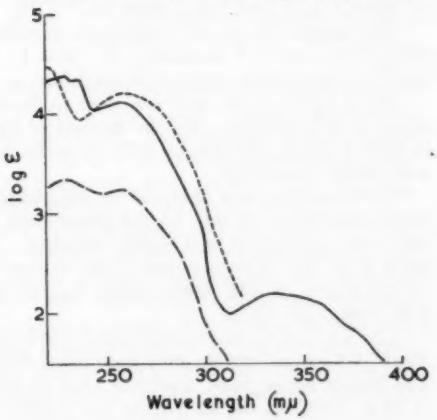


FIG. 3. (II; $n = 1$) (——) *in methylcyclohexane.* (II; $n = 3$) (– – – –) *in methylcyclohexane.* 3,4,3′,4′-*Tetrahydro*-1,1′-*binaphthyl* (. . . .).[15]

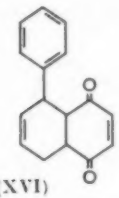


absence of a quinonoid system. However, on the basis of existing evidence it is not possible to differentiate unambiguously between structures (VII) and (VIIa). Braude *et al.*[11] report $\lambda_{max.}$ 220, 250, 256 (ε 15,500, 1450, 1400) for system (XVI). Bastron *et al.*[12] report

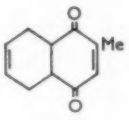
[11] Braude, Jones, and Stern, *J.*, 1947, 1092.
[12] Bastron, Davis, and Butz, *J. Org. Chem.*, 1943, **8**, 515.

XUM

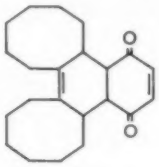
$\lambda_{max.}$ 237, 354 (ε 12,250, 62) for system (XVII). On the other hand, Strumza and Ginsburg [13] found no maximum in the 220—260 mμ region in system (XVIII); and Mandelbaum and Cais [14] found no maximum in this region in system (XIX).



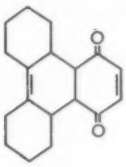
(XVI)



(XVII)



(XVIII)



(XIX)

It is interesting that a large hypochromic effect is shown in the spectrum of the diene (II; $n = 3$) as compared with those of (II; $n = 1$) and of 3,4,3′,4′-tetrahydro-1,1′-binaphthyl [15] * (see Fig. 3).

Experimental

1,1′-*Bi-indanyl*-1,1′-*diol* (I; $n = 1$).—A mixture of freshly scraped aluminium foil (8 g.; 1 cm.² squares, 0·005 inch thick), indan-1-one (25 g.), mercuric chloride (0·5 g.), dry ethanol (200 ml.), and dry benzene (250 ml.) was heated on the steam-bath for 12 hr. away from light (indan-1-one in solution is sensitive to light). After cooling, the excess of aluminium was dissolved in cold 20% Rochelle salt solution (400 ml.) with cooling. The aqueous phase was extracted with ether (3 × 150 ml. portions), and the combined organic phases were washed with Rochelle salt solution until the aqueous phase was clear. After drying (Na_2SO_4) and removal of the solvents, a mixture of methylcyclohexane (30 ml.) and benzene (30 ml.) was added and the solution was refrigerated overnight. The crystalline *pinacol* removed by filtration (9·5 g., 38%) had m. p. 152—154°. The analytical sample (from methylcyclohexane) formed needles; m. p. 156—157° (Found: C, 80·9; H, 6·9; O, 12·1. Calc. for $C_{18}H_{18}O_2$: C, 81·2; H, 6·8; O, 12·0%), $\nu_{max.}$ (in $CHCl_3$), 3600 cm.$^{-1}$ (OH).

The mother-liquor, on distillation, afforded unchanged indanone, b. p. 70—80°/0·05 mm. (1·2 g., 5%), and 3,3′-bi-indenyl (II; $n = 1$), b. p. 146—148°/0·05 mm. (6·9 g., 32%), a yellow solid. Crystallisation gave yellowish prisms, m. p. 131° (from ethanol) (lit.,[5] m. p. 130·5—131·5°).

When hydrochloric acid was used to dissolve the excess of aluminium, none of the above products was isolated. By the method of Barnett and Lawrence [2] the pinacol was isolated in 25% yield in addition to 10% of unchanged indanone; the reddish residue did not react with maleic anhydride.

3,3′-Bi-indenyl was obtained by dehydration of the diol (13 g.) by acetic acid (22 ml.) and acetic anhydride (22 ml.) on the steam-bath in 1 hr. Water was added to the hot solution until the appearance of a slight turbidity. Refrigeration and filtration afforded crystalline diene (8 g.) and concentration of the mother-liquor gave a second crop (1·5 g.). The hydrocarbon had m. p. 131° (84% yield), $\lambda_{max.}$ (in methylcyclohexane) 228, 236, 257, 340 mμ (log ε 4·39, 4·36, 4·10, 2·17).

5,5a,6,7,7a,8-*Hexahydroindeno*[2,1-*c*]*fluorene*-6,7-*dicarboxylic Anhydride* (III).—The above diene (1·5 g.) and maleic anhydride (5 g.) were heated under reflux in xylene (25 ml.) for 3 hr. The adduct began to be deposited after 15 min. Cooling and filtration gave colourless needles (1·26 g., 59%) of the anhydride, m. p. 310° (lit., m. p. 310°,[5] 300—302°) [6] (Found: C, 79·7; H, 4·95. Calc. for $C_{22}H_{16}O_3$: C, 80·5; H, 4·9%), $\nu_{max.}$ (in KBr) 1860, 1780 cm.$^{-1}$ (C=O of carboxylic anhydride), $\lambda_{max.}$ (in dioxan) 231—232, 242, 252, 292, 304, 331, 346 mμ (log ε 4·15, 4·13, 3·99, 3·95, 3·99, 4·41, 4·41).

* We thank Dr. M. Cais for discussion of the ultraviolet spectra.

[13] Strumza and Ginsburg, unpublished work.
[14] Mandelbaum and Cais, personal communication.
[15] Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," Wiley, New York, 1951, Spectrum No. 121.

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Removal of the solvent from the mother-liquor and trituration of the residue with methanol (which dissolved the excess of maleic anhydride) gave a second isomer as yellow needles (230 mg., 11%), m. p. 262° (from benzene or acetic acid) (lit., m. p. 262°,[5] 255—265 °) (Found: C, 80·3; H, 5·0. Calc. for $C_{22}H_{16}O_3$: C, 80·5; H, 4·9%), $\nu_{max.}$ (in KBr) 1870, 1790 cm.$^{-1}$, $\lambda_{max.}$ (in dioxan) 231, 242, 252, 293, 331, 347 mμ (log ε 4·21, 4·09, 3·97, 3·98, 4·43, 4·41).

5,8-*Dihydroindeno*[2,1-*c*]*fluorene* (IV).—A finely powdered mixture of the anhydride (III) (100 mg.), copper powder (100 mg.), barium hydroxide (200 mg.; dried at 400° for 12 hr.), and soda-glass (500 mg.) was heated slowly to 400° and kept at 400° for 1 hr. in an inert atmosphere. The hydrocarbon sublimed. After cooling, the residue was extracted with hot methylcyclohexane, and the combined extracts were passed over a column of acid-washed alumina (5 g.) and eluted with hexane. The yellowish products gave colourless needles of the hydrocarbon, m. p. 144—145° (from ethanol) (lit.,[6] m. p. 140—142°). The yield varied from 10% to 50% and decreased when larger batches were decarboxylated.

Decarboxylation by Deuschel's procedure [6] with palladised carbon at 240°/120 mm. was unsuccessful in our hands. This catalyst (500 mg.) and the dione (V), heated for 8 hr. at 400°/1 atm. (inert gas), gave the hydrocarbon, m. p. 144—145° (80 mg., 20%), $\lambda_{max.}$ (in methylcyclohexane) 245, 262, 277, 304, 314 mμ (log ε 4·07, 4·37, 4·07, 4·33, 4·35).

5,8-*Dihydro*-5,8-*dioxoindeno*[2,1-*c*]*fluorene* (V).—A mixture of the hydrocarbon (IV) (100 mg.), sodium dichromate (336 mg.), and acetic acid (2·5 ml.) was refluxed for 2 hr. After cooling, water and chloroform were added and the coloured chloroform layer was washed with sodium hydrogen carbonate solution and with water until it remained colourless. After drying (Na_2SO_4) and removal of solvent a yellow residue (101 mg.), m. p. 244—274°, was obtained. It was dissolved in benzene (2 ml.) and chloroform (2 ml.), passed over a column of basic alumina (10 g.), and eluted with benzene–chloroform (2 : 1). After a first impure fraction (9 mg.), the *diketone* was obtained (89 mg.) as yellow needles, m. p. 281—283° (from benzene) (Found: C, 85·4; H, 3·6; O, 11·3. $C_{20}H_{10}O_2$ requires C, 85·1; H, 3·6; O, 11·4%), $\nu_{max.}$ (in $CHCl_3$) 1710—1725 cm.$^{-1}$ (C=O), $\lambda_{max.}$ (in dioxan) 282, 311, 367, 390 (mμ) (log ε 4·42, 4·60, 3·34, 3·00).

5,5a,6,9,9b,10-*Hexahydrodi-indeno*[2,1-*a*,1,2-*c*]*naphthalene*-6,9-*dione* (VI).—The diene (II; $n = 1$) (1·8 g.) and *p*-benzoquinone (2·2 g.) were heated in acetic acid (25 ml.) on the steam-bath for 15 min. Filtration of the deposited red crystals and washing with ethanol to remove quinhydrone afforded the *diketone* (700 mg., 41%) as red needles, m. p. 240—242° (decomp.; in evacuated capillary) (from xylene) (Found: C, 85·85; H, 4·65. $C_{24}H_{16}O_2$ requires C, 85·7; H, 4·8%), $\nu_{max.}$ (in KBr) 1653 cm.$^{-1}$ (quinonoid C=O), $\lambda_{max.}$ (in dioxan) 232, 257, 295, 405 mμ (log ε 4·48, 4·46, 4·43, 4·09).

9,9a,9b,10,10a,10b,11,20,20a,20b,21,21a,21b,22-*Tetradecahydrotetraindeno*[2,1-*a*:1′,2′-*c*:2″,1″-*h*:1‴:2‴-*j*]*anthracene*-10,21-*dione* (VII).—A mixture of the diene (II; $n = 1$) (4·2 g.) and *p*-benzoquinone (0·98 g.) was boiled in acetic acid (40 ml.) for 1 hr. After cooling, yellow needles of the *diketone* were deposited, having m. p. 278° (decomp.; in evacuated capillary) (from xylene) (Found: C, 89·2; H, 5·4; O, 5·5. $C_{42}H_{32}O_2$ requires C, 88·7; H, 5·7; O, 5·6%), $\nu_{max.}$ (in KBr) 1680 cm.$^{-1}$ (C=O), $\lambda_{max.}$ (in dioxan) 232, 297, 330 mμ (log ε 4·60, 4·71, 4·57).

2,3:2′,3′-*Dibenzobi*(*cyclohepta*-2,7-*dienyl*) (II; $n = 3$).—A mixture of aluminium foil (6 g.; as above), benzocyclohepten-3-one (20 g.), mercuric chloride (0·5 g.), dry ethanol (80 ml.), and dry benzene (120 ml.) was heated on a steam-bath for 12 hr. After cooling, the excess of aluminium was dissolved in cold 10% hydrochloric acid. The aqueous phase was extracted several times with benzene–ether (1 : 1), and the combined organic phases were washed once with 10% hydrochloric acid. After removal of the solvents, acetic acid (45 ml.) and acetic anhydride (45 ml.) were added to the residue and the solution was refluxed for 3 hr. to complete dehydration of the pinacol. Removal of the solvents at reduced pressure followed by distillation gave unchanged ketone (2 g.), b. p. 75—80°/0·05 mm., and the *diene* (13·5 g., 75%), b. p. 156—160°/0·05 mm. Crystallisation afforded colourless prisms, m. p. 96° (from propan-2-ol) (Found: C, 92·4; H, 7·7. $C_{22}H_{22}$ requires C, 92·3; H, 7·7%); $\lambda_{max.}$ (in methylcyclohexane) 233, 257 mμ (log ε 3·32, 3·21).

2,3:2′,3′-*Dibenzobi*(*cyclohepten*-1-*yl*)-1,1′-*diol* (I; $n = 3$) was isolated when hexane was added to the residue before dehydration, as colourless needles (8 g., 40%), m. p. 214° (from benzene or methylcyclohexane) (Found: C, 81·9; H, 8·4; O, 9·85. $C_{22}H_{26}O_2$ requires C, 81·95; H, 8·1; O, 9·9%), $\nu_{max.}$ (in $CHCl_3$) 3600 cm.$^{-1}$ (OH).

Reduction by the procedure of Barnett and Lawrence [2] gave the pinacol in 10% yield,

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benzocyclohepten-3-ol, m. p. 103°, in 10% yield (lit.,[16] m. p. 101°), and unchanged ketone (11%). The reddish residue did not react with maleic anhydride.

5,6,7,7a,8,9,9a,10,11,12-*Decahydrodi*(*benzocycloheptа*)[6,5-*a*:5′,6′-*c*]*benzene*-8,9-*dicarboxylic Anhydride* (VIII).—The diene (II; $n = 3$) (1·5 g.), when heated on the steam-bath with maleic anhydride (7·5 g.), gave a melt which began depositing crystals after 30 min. After 3 hours' heating, hot acetic acid or acetic anhydride was added to dissolve the excess of maleic anhydride. On cooling, the *anhydride adduct* was obtained (1·35 g., 65%), having m. p. 257° (from acetic anhydride or acetic acid) (Found: C, 81·2; H, 6·5. $C_{26}H_{24}O_3$ requires C, 81·2; H, 6·3%), $\nu_{max.}$ (in $CHCl_3$) 1870, 1780 cm.$^{-1}$ (C=O of carboxylic anhydride), $\lambda_{max.}$ (in dioxan) 229, 275 mμ (log ε 4·18, 4·03).

5,6,7,10,11,12-*Hexahydrodi*(*benzocycloheptа*)[6,5-*a*:5′,6′-*c*]*benzene* (IX).—A finely powdered mixture of the anhydride (VIII) (500 mg.) and lead dioxide (1·34 g.; Fisher, technical) in freshly distilled decalin (4 ml.) was heated to 190—200° in an inert atmosphere. Carbon dioxide was evolved during 3 hr. (barium hydroxide solution). The mixture was cooled to 100°, 2,2,4-trimethylpentane (10 ml.) was added, and refluxing maintained for 10 min. The liquid was decanted and this extraction was repeated twice more. Finally the solid was removed and washed with ether. The organic extracts were combined and the solvents removed in a vacuum. The residual oil was triturated with pentane to give a yellow solid. Sublimation at 160°/0·5 mm. gave the colourless *hydrocarbon* (225 mg., 56%), needles, m. p. 194° (from ethanol) (Found: C, 92·95; H, 7·25. $C_{24}H_{22}$ requires C, 92·9; H, 7·1%), $\lambda_{max.}$ (in methylcyclohexane) 221, 245, 265 mμ (log ε 4·53, 4·48, 4·12).

5,6,7,10,11,12-*Hexahydrodi*(*benzocycloheptа*)[6,5-*a*:5′,6′-*c*]*benzene*-8,9-*dicarboxylic Anhydride* (X).—A mixture of the anhydride (VIII) (550 mg.), fresh lead tetra-acetate (1·4 g.), acetic acid (7 ml.), and acetic anhydride (7 ml.) was heated at 120° for 2 hr. Water was added dropwise to the hot solution until a slight turbidity appeared. After cooling, yellow crystals, m. p. 244—276°, were deposited. Four recrystallisations raised the m. p. to 284—285° (from acetic anhydride) (390 mg., 72%) (Found: C, 81·4; H, 5·55; O, 13·0. $C_{26}H_{20}O_3$ requires C, 82·0; H, 5·3; O, 12·6%), $\nu_{max.}$ (in $CHCl_3$) 1850, 1770 cm.$^{-1}$ (C=O of carboxylic anhydride), $\lambda_{max.}$ (in dioxan) 269, 337 mμ (log ε 4·51, 4·02).

Dimethyl 5,6,7,7a,9a,10,11,12-*Octahydrodi*(*benzocycloheptа*)[6,5-*a*:5′,6′-*c*]*benzene*-8,9-*dicarboxylate* (XI).—A mixture of the diene (II; $n = 3$) (1 g.) and freshly distilled dimethyl acetylenedicarboxylate (5·2 g.) was heated on the steam-bath for 24 hr. The excess of dienophile was removed in a vacuum and the residue was triturated with methanol. The *diester* was obtained as colourless plates, m. p. 225° (from propan-1-ol) (870 mg., 58%) (Found: C, 78·05; H, 7·1. $C_{28}H_{28}O_4$ requires C, 78·5; H, 6·6%), $\nu_{max.}$ (in $CHCl_3$) 1720 cm.$^{-1}$ (C=O of ester).

Hydrolysis of the ester (300 mg.) was effected in aqueous (1·5 ml.)–methanolic (7 ml.) dioxan (7 ml.) by boiling in the presence of potassium hydroxide (1·5 g.) for 15 hr. After the usual working up, the product (240 mg., 90%) had m. p. 272° (needles from acetic acid or n-butyl acetate). Infrared absorption (in $CHCl_3$) at 1850, 1770 cm.$^{-1}$ indicated that the product was 5,6,7,7a,9a,10,11,12-*octahydrodi*(*benzocycloheptа*)[6,5-*a*:5′,6′-*c*]*benzene*-8,9-*dicarboxylic anhydride* (XII) (Found: C, 81·0; H, 6·0; O, 13·1. $C_{28}H_{22}O_3$ requires C, 81·65; H, 5·8; O, 12·25%); ultraviolet absorption max. (in dioxan) were at 253, 325 mμ (log ε 4·13, 3·94).

5,6,7,7a,7b,8,11,11a,11b,12,13,14-*Dodecahydrodi*(*benzocycloheptа*)[6,5-*a*:5′,6′-*c*]*naphthal ene* 8,11-*dione* (XIII) *and* 5,6,7,7a,8,11,11b,12,13,14-*Decahydrodi*(*benzocycloheptа*)[6,5-*a*:5′,6′-*c*]-*naphthalene*-8,11-*dione* (XIV).—A mixture of the diene (II; $n = 3$) (3·6 g.) and *p*-benzoquinone (5·6 g.) was heated in acetic acid (60 ml.) on the steam-bath for 3 hr., then cooled overnight. Quinhydrone was precipitated along with orange crystals of compound (XIV). The product (XIII) was found in the mother-liquor. Washing the precipitate with cold ethanol removed quinhydrone only, and the *adduct* (XIV) gave orange needles (0·5 g., 10%), m. p. 271° (from acetic acid) (Found: C, 85·2; H, 6·4. $C_{28}H_{24}O_2$ requires C, 85·7; H, 6·2%), $\nu_{max.}$ (in $CHCl_3$) 1655, (in KBr) 1650 cm.$^{-1}$ (quinonoid C=O), $\lambda_{max.}$ (in dioxan) 247, 300infl., 338 mμ (log ε 4·08, 3·14, 3·01).

The acetic acid was removed from the mother-liquor, and the residue was dissolved in benzene–hexane (1 : 1). Quinhydrone was precipitated and was removed. The solution was then washed with 5% sodium dithionite solution to convert quinhydrone into quinol, then with 5% sodium hydrogen carbonate solution to remove the latter. After drying (Na_2SO_4) and removal of solvents, the residue was triturated with methanol and gave yellow needles of the *adduct* (XIII) (2·6 g., 54%), m. p. 210° (from propan-1-ol) (Found: C, 84·85; H, 6·9;

[16] Horn and Rapson, *J.*, 1949, 2426.

O, 8·15. $C_{28}H_{26}O_2$ requires C, 85·2; H, 6·6; O, 8·1%), $\nu_{max.}$ (in $CHCl_3$) 1695 (C=O), (in KBr) 1680 cm.$^{-1}$, $\lambda_{max.}$ (in dioxan) 224, 297infl. mμ (log ε 4·42, 3·00).

Compound (XIII) has a potential enolic function. Boiling with ethanolic sodium ethoxide for 15 min. followed by the usual working up give the *dihydric phenol* (XV; R = H), m. p. 296° (from toluene) (Found: C, 85·0; H, 6·6. $C_{28}H_{28}O_2$ requires C, 85·2; H, 6·6%), $\nu_{max.}$ (in KBr) 3330 cm.$^{-1}$ (OH of phenol) [*diacetate*, m. p. 283—284° (from toluene) (Found: C, 80·1; H, 6·1; O, 13·3. $C_{32}H_{32}O_4$ requires C, 80·3; H, 6·3; O, 13·4%), $\nu_{max.}$ (in $CHCl_3$) 1760 cm.$^{-1}$ (C=O of ester)].

When heated with an excess of *p*-benzoquinone for 8 hr., the monoadduct (XIII) gave the quinone (XIV).

If the time of heating of the diene (II; $n = 3$) with *p*-benzoquinone was increased, *e.g.*, to 8 hr., the quinone (XIV) was obtained in higher yield (30%) at the expense of the monoadduct (33%).

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Haifa, Israel. [*Received, September 8th*, 1960.]

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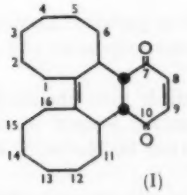
294. *Alicyclic Studies. Part XVI.* The Diels–Alder Reaction of Bi(cyclo-oct-1-enyl) with* p-*Benzoquinone and Steric Interconversions of the Primary Adduct.*†

By Jacob Strumza and David Ginsburg.

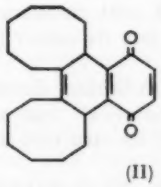
The reaction between bi(cyclo-oct-1-enyl) and *p*-benzoquinone gives a Diels–Alder adduct. Various reactions of the adduct and steric relations between its derivatives are described.

Diels–Alder reactions of symmetrical bicyclic dienes have been described previously.[1] When two equivalents of bi(cyclo-oct-1-enyl) are heated with one of *p*-benzoquinone it is possible to isolate in high yield a 1 : 1 adduct (I) having the usual *cis*-fusion between the two six-membered rings. Spectroscopic and analytical data are consistent with this structure.

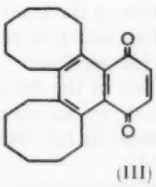
The pure diketone is stable at room temperature but heat or base readily isomerises



(I)



(II)



(III)

it to the dihydric phenol (IV).[1] Acetic anhydride and acetic acid convert it into the diacetate (XVII), identical with the product of acetylation of the phenol.

The driving force of aromatisation does not exist in quinonoid systems such as (II) and (III) which may be obtained by allowing an excess of *p*-benzoquinone to react in acetic acid solution [2] either directly with bi(cyclo-oct-1-enyl) or with the adduct (I) or (II), respectively. The infrared absorptions of the carbonyl systems of compounds (II) and (III) (1653 and 1650 cm.$^{-1}$) are in accord with their quinonoid structure. The quinone

* Part XV, preceding paper.
† Presented at Colloque International de Stereochimie, Montpellier, September, 1959.

[1] Greidinger and Ginsburg, *J. Org. Chem.*, 1957, **22**, 1406 and papers cited therein.
[2] Davies and Porter, *J.*, 1957, 4961, 4967.

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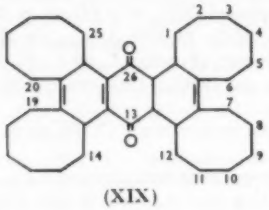
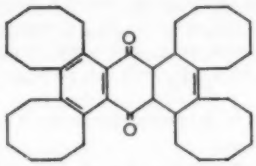
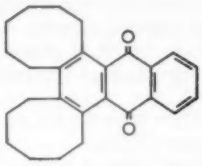
(II) can be reduced to the quinol (IV) by zinc in acetic acid,[3] and the reverse transformation can be accomplished by oxidation with the chromium trioxide–pyridine complex.



(XIX)



(XX)



(XXI)

The activated double bond in the quinones (II) and (III), flanked by two carbonyl functions, adds to another mole of bi(cyclo-oct-1-enyl), giving the two bis-adducts (XIX) and (XX), respectively. Further dehydrogenation of these adducts with an excess of *p*-quinone could not be achieved. An annelated anthraquinone (XXI) was, however, obtained by *p*-quinone dehydrogenation of the bi(cyclo-oct-1-enyl)–naphthaquinone adduct (see Experimental section).

Reduction of the diketone (I) with lithium aluminium hydride gave an unsaturated diol (VII), dehydration of which in 85% phosphoric acid led to a hydrocarbon (XV) that could be further dehydrogenated to give the dodecahydrodicyclo-octa[*a*,*c*]naphthalene (XVI). The 1,4-diacetoxy-derivative (XVIII) of the latter was analogously obtained.

Stereochemical Correlations.—It appeared desirable to establish the steric relations of the six-membered ring portions of the compounds described below in the hope that later, by introduction of functional groups into the eight-membered rings and interaction between the various parts of the molecules, a contribution might be made to the conformation of the eight-membered ring. Accordingly, the following transformations were carried out (cf. reaction chart [*]).

It has been shown that reduction of the type (I) ⟶ (V) with zinc in acetic acid does not affect the fusion of the six-membered rings.[4-6] The product (V) showed saturated carbonyl character ($\nu_{max.}$ 1708 cm.$^{-1}$) in its infrared spectrum. Base epimerised it to the *trans*-fused diketone (IX). Catalytic reduction of either diketone (I) or (V) afforded a *cis*-fused ketol (VI),[6a] and this was epimerised by sodium methoxide to the *trans*-fused ketol (XII), where, however, a double bond had migrated.

Oxidation of the *trans*-ketol (XII) with chromium trioxide in pyridine gave a diketone (XIV). This could be reconverted into its isomer (IX) by rearrangement of the double bond in acidic medium.

Reduction of the diketone (I) with lithium aluminium hydride gave the *cis*-ketol (VI) accompanied by an unsaturated diol (VII) and an unidentified isomer of the latter. The *cis*-fusion in the diol (VII) and its structure are supported by the work of several authors.[4,7,8]

By further reducing the diketone (V) or (VI) with lithium aluminium hydride or by adding one mol. of hydrogen catalytically to the diol (VII), the same *cis*-fused saturated diol (VIII) was obtained.

Although oxidation of the diol (VII) with chromic acid–pyridine gives the quinone (II), both compounds (VI) and (VIII) gave with this reagent the corresponding diketone (V).

[*] All the compounds are optically inactive, and braces indicate eight-membered rings.

[3] Cf. Alder and Stein, *Annalen*, 1933, **501**, 247.
[4] Sarett, Lukes, Poos, Robinson, Beyler, Vandegrift, and Arth, *J. Amer. Chem. Soc.*, 1952, **74**, 1393.
[5] Henbest, Smith, and Thomas, *J.*, 1958, 3293.
[6] Robins and Walker, (*a*) *J.*, 1952, 642, 1610; (*b*) *J.*, 1957, 177; (*c*) *J.*, 1958, 409.
[7] Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.
[8] Robins and Walker, (*a*) *J.*, 1959, 237; (*b*) *J.*, 1954, 3960; (*c*) *J.*, 1955, 1789.

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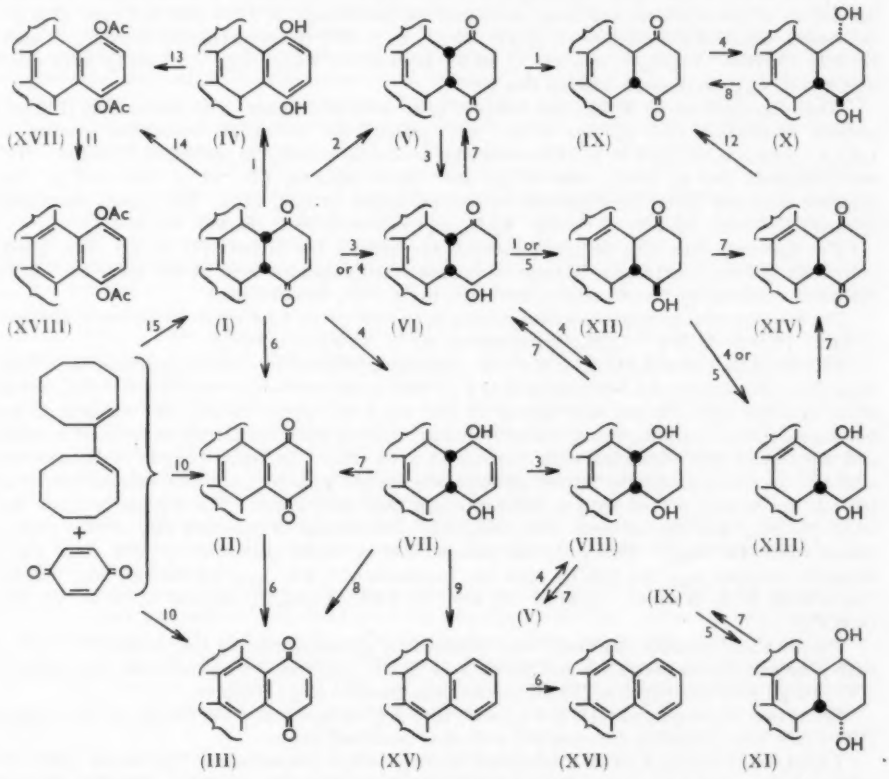
Reduction of the *trans*-diketone (IX) with metal hydrides gave a mixture of diastereoisomeric diols (X) and (XI), formulated as the diequatorial and the diaxial isomers, respectively (see Experimental section). Attempts to obtain the equatorial-axial isomer failed. Metal hydride reduction of the ketol (XII) afforded a third *trans*-fused diol (XIII) which



Reagents: 1, NaOMe; 2, Zn–AcOH; 3, H_2–Pt; 4, $LiAlH_4$; 5, $NaBH_4$; 6, benzoquinone–AcOH; 7, CrO_3–pyridine; 8, CrO_3–AcOH; 9, 85% H_3PO_4; 10, AcOH; 11, 30% Pd–C; 12, 2-$C_{10}H_7$·SO_3H; 13, Ac_2O–pyridine; 14, Ac_2O–H^+; 15, Heat.

differs, however, from the diols (X) and (XI) in the location of its double bond. The last two, (X) and (XI), were reoxidised with chromic oxide in pyridine or in acetic acid to the same diketone (IX) whilst oxidation of the isomer (XIII) led to a correspondingly isomeric diketone (XIV).

Since conclusions regarding the configurations of the hydroxyl groups in the above-mentioned diols could not be drawn from infrared data in the 1000 $cm.^{-1}$ region, kinetic experiments were carried out.

Oxidation rates, kindly determined by Dr. J. Schreiber at E.T.H., Zürich, showed a higher value for the diol (XI), in accordance with its diaxial formulation.[9,10] Further, the diacetate of the diol (X), formulated as the diequatorial isomer, was hydrolysed faster than the diacetate of (XI). The diol (X) distinctly showed a higher polar character than (XI), on elution of a mixture of the two isomers from the chromatographic column.[9,11]

[9] Barton, *Experientia*, 1950, **6**, 316.
[10] Schreiber and Eschenmoser, *Angew. Chem.*, 1955, **67**, 278.
[11] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.

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Experimental

$\Delta^{8,16a(16b)}$-*Octadecahydrodicyclo-octa*[a,c]*naphthalene*-7,10-*dione* (I).—Pure *p*-benzoquinone (3·5 g., 0·031 mole) was dissolved in bicyclo-oct-1-enyl (14 g., 0·064 mole) by gentle heating on a steam-bath. Within 5 min., though overheating was avoided, a strong exothermic reaction took place and the red liquid changed to a yellow solid. Trituration with methanol dissolved the excess of diene which was later recovered by distillation at 118—120°/0·2 mm. (3·6 g.); the residue afforded the *diketone* (I) (9·3 g., 89%), m. p. 135° (from methanol) (Found: C, 80·7; H, 9·2; O, 10·6. $C_{22}H_{30}O_2$ requires C, 80·9; H, 9·3; O, 9·8%), $\nu_{max.}$ (in $CHCl_3$) 1675 cm.$^{-1}$ (C=C·C=O), $\lambda_{max.}$ (in dioxan) 328 mμ (log ε 2·78).

When the diketone (I) (0·5 g.) was refluxed in an inert atmosphere with methanolic (100 ml.) sodium methoxide (0·5 g.) for 1 hr. and worked up as usual, colourless needles of 1,2,3,4,5,6,6a,10b,11,12,13,14,15,16-tetradecahydrodicyclo-octa[*a,c*]naphthalene-7,10-diol (IV) were obtained (0·3 g., 60%), with m. p. 187° (from benzene) (lit., m. p. 187—188°). The *diacetate* obtained from the diphenol formed colourless prisms, m. p. 155° (from methanol) (Found: C, 75·95; H, 8·6; O, 15·55. $C_{26}H_{34}O_4$ requires C, 76·1; H, 8·3; O, 15·6%).

The diacetate was also obtained directly by heating the adduct (I) (1 g.) with acetic anhydride (20 ml.) containing 3 drops of concentrated sulphuric acid at 90° for 1 hr. After the usual working-up, the diacetate (480 mg.), m. p. 155°, was obtained.

The *dimethyl ether* formed colourless prisms, m. p. 169° (from 2,2,4-trimethylpentane) (Found: C, 81·2; H, 9·6; O, 9·2. $C_{24}H_{34}O_2$ requires C, 81·3; H, 9·7; O, 9·0%).

1,2,3,4,5,6,6a,7,10,10b,11,12,13,14,15,16-*Hexadecahydrodicyclo-octa*[a,c]*naphthalene*-7,10-*dione* (II).—A solution of *p*-benzoquinone (1 g., 0·0092 mole) and bicyclo-oct-1-enyl (0·5 g., 0·0023 mole) in acetic acid (10 ml.) was heated at 100° for 3 hr. After cooling and removal of the black precipitate of quinhydrone, the solvent was removed from the filtrate at reduced pressure and the residue was extracted with benzene (3 × 50 ml.). An equal volume of hexane was added to the extracts and the filtered solution was washed with 40% aqueous sodium hydroxide (40 ml.) containing 5% of sodium dithionite and then with water. The organic solution was dried (Na_2SO_4) and the solvents were removed. Trituration of the dark oily residue gave a brown solid (430 mg.). This gave the *quinone* (II) as brown plates, m. p. 104—105° (from ethanol; carbon), $\nu_{max.}$ (in $CHCl_3$) 1653 cm.$^{-1}$ (quinonoid C=O), $\lambda_{max.}$ (in dioxan) 256, 365 mμ (log ε 4·15, 3·17) (Found: C, 81·5; H, 8·8; O, 10·0. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7; O, 9·9%).

The identical quinone (350 mg.) was obtained by dehydrogenating the product (I) (0·5 g.) with *p*-benzoquinone (0·5 g.) in hot acetic acid (5 ml.) for 8 hr. or by oxidising the diphenol (IV) (0·5 g.) with the pyridine (10 ml.)–chromium trioxide (1 g.) complex.

Reduction of the quinone (II) (0·5 g.) with zinc (4 g.) in acetic acid (40 ml.) gave the diphenol (XIV) (250 mg.), identical (admixture) with that described above.

1,2,3,4,5,6,11,12,13,14,15,16-*Dodecahydrodicyclo-octa*[a,c]*naphthalene*-7,10-*dione* (III).—A mixture of pure *p*-benzoquinone (1 g., 0·0092 mole), bicyclo-oct-1-enyl (0·5 g., 0·0023 mole) and acetic acid (10 ml.) was heated at 100° for 8 hr. The mixture was cooled, the precipitate removed, and the filtrate extracted with benzene. An equal volume of hexane was added to the benzene solution and the mixture was washed with alkaline sodium dithionite solution and with water. After drying (Na_2SO_4) and removal of the solvents, trituration with methanol gave a yellow solid (280 mg.), forming golden needles of the *diketone*, m. p. 151—152° (from ethanol, carbon), $\nu_{max.}$ (in $CHCl_3$) 1655 cm.$^{-1}$ (quinonoid C=O), $\lambda_{max.}$ (in dioxan) 260, 381 mμ (log ε 4·28, 3·67) (Found: C, 81·9; H, 8·2; O, 10·0. $C_{22}H_{26}O_2$ requires C, 81·95; H, 8·1; O, 9·9%).

The identical diketone (III) (300 mg.) was obtained by dehydrogenating the product (II) (0·5 g.) with *p*-benzoquinone (2 g.) in acetic acid (5 ml.).

cis-$\Delta^{16a(16b)}$-*Eicosahydrodicyclo-octa*[a,c]*naphthalene*-7,10-*dione* (V).—To a solution of the product (I) (2 g.) in 95% acetic acid (80 ml.) was added in small portions, with stirring during 1 hr., zinc dust (16 g.) that had been previously washed with chloroform and ether. Decolorisation occurred within a few minutes. This mixture was filtered into ice-cold saturated salt solution and this was extracted with ether (500 ml.). The organic layer was washed successively with salt solution and aqueous sodium hydrogen carbonate until free from acid. After drying (Na_2SO_4) and removal of the ether the residue was triturated with pentane, affording colourless cubes (1·7 g., 85%) of the cis-*diketone*, m. p. 108° (from pentane), $\nu_{max.}$ (in $CHCl_3$) 1708 cm.$^{-1}$ (saturated C=O), $\lambda_{max.}$ (in dioxan) 297 mμ (log ε 2·07) (Found: C, 80·4; H, 9·8; O, 9·95.

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$C_{22}H_{32}O_2$ requires C, 80·4; H, 9·8; O, 9·7%). The *bis*-2,4-*dinitrophenylhydrazone* formed brown needles, m. p. 265° (decomp.), from chloroform–methanol (Found: N, 16·1. $C_{34}H_{40}N_8O_8$ requires N, 16·3%).

Epimerisation was effected by adding the diketone (V) (1·2 g.) to a solution prepared from sodium (0·5 g.) and dry methanol (100 ml.) and refluxing the whole in an inert atmosphere for 1 hr. After the usual working-up, the trans-*diketone* (IX) (300 mg., 40%) formed needles, m. p. 145—146° (from hexane). Removal of the solvent from the mother-liquor and refluxing of the residue, m. p. 120—125° (700 mg.), in benzene (50 ml.) with naphthalene-β-sulphonic acid (300 mg.) afforded the same diketone, m. p. 145° (from hexane). It had $\nu_{max.}$ (in $CHCl_3$) 1705 $cm.^{-1}$ (saturated C=O) and $\lambda_{max.}$ (in dioxan) 300 mμ (log ε 1·68) (Found: C, 80·3; H, 9·7; O, 10·6%). The *mono*-2,4-*dinitrophenylhydrazone* formed yellow needles, m. p. 230° (decomp.), from chloroform–methanol (Found: N, 11·2. $C_{28}H_{36}N_4O_5$ requires N, 11·0%).

cis-$\Delta^{16\alpha(16b)}$-*Eicosahydro*-10-*hydroxydicyclo-octa*[a,c]*naphthalene*-7-*one* (VI).—A solution of the product (I) (4 g.) in ethyl acetate (150 ml.) was reduced at atmospheric pressure over Adams catalyst (400 mg.), 2 mol. of hydrogen (320 ml.) being taken up during 3 hr. Removal of catalyst and concentration afforded colourless prisms of the *ketol* (VI) (1·5 g., 38%), m. p. 174° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3550, 1025 (OH), 1710 $cm.^{-1}$ (saturated C=O), $\lambda_{max.}$ (in dioxan) 290 mμ (log ε 1·43) (Found: C, 79·9; H, 10·1; O, 9·5. $C_{22}H_{34}O_2$ requires C, 79·95; H, 10·4; O, 9·7%).

Evaporation of the solvent and trituration of the residual oil with benzene afforded the diphenol (IV) (2·1 g.), m. p. 184° (from benzene). Removal of the benzene and trituration with methanol yielded more of the ketol (VI) (0·25 g.; total yield 43%).

The *ketol monoacetate* formed cubes, m. p. 140° (from ethanol), $\nu_{max.}$ (in $CHCl_3$) 1725 (ester C=O), 1710 $cm.^{-1}$ (saturated C=O) (no OH absorption) (Found: C, 76·9; H, 9·8; O, 13·2. $C_{24}H_{36}O_3$ requires C, 77·4; H, 9·7; O, 12·9%). The *ketol monoacetate* 2,4-*dinitrophenylhydrazone* formed yellow needles, m. p. 245° (decomp.) from ethyl acetate (Found: C, 65·2; H, 7·4; N, 10·1. $C_{30}H_{40}N_4O_6$ requires C, 65·2; H, 7·3; N, 10·1%).

The identical (mixed m. p. and infrared spectrum) ketol (VI) was obtained (70% yield) by reducing the diketone (V) (100 mg.) in ethyl acetate (10 ml.) in the presence of Adams catalyst (20 mg.) during 3 hr.

Epimerisation was effected by refluxing a solution of the ketol (VI) (1·5 g.) with methanolic (300 ml.) sodium methoxide (prepared from 0·8 g. of sodium) for 1 hr. After the usual working-up the trans-*ketol* (XII) (1·3 g., 87%) was obtained as plates, m. p. 168° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3600 (OH), 1700 $cm.^{-1}$ (saturated C=O), $\lambda_{max.}$ (in dioxan) 290 mμ (log ε 1·52) (Found: C, 79·55; H, 10·3; O, 9·71%). The *mono*-2,4-*dinitrophenylhydrazone*, orange needles, had m. p. 135° (from ethanol) (Found: C, 66·0; H, 7·4; O, 15·7; N, 10·85. $C_{28}H_{38}N_4O_5$ requires C, 65·9; H, 7·5; O, 15·7; N, 11·0%). The identical derivative was obtained from the ketol (VI). The *monoacetate* from the *trans*-isomer (XII) proved identical with that obtained from (VI) (see above). Evidently epimerisation of (VI) takes place during acetylation and during formation of its 2,4-dinitrophenylhydrazone.

$\Delta^{8,16\alpha(16b)}$-*Octadecahydrodicyclo-octa*[a,c]*naphthalene*-7,10-*diol* (VII).—A solution of product (I) (5 g.) in dry ether (200 ml.) was added during 30 min. to lithium aluminium hydride (7·5 g.) in dry ether (200 ml.) with stirring. The mixture was refluxed for 5 hr. and left overnight. After decomposition by water and dilute sulphuric acid and the usual working-up, trituration with methanol gave colourless crystals (2·42 g.). Five recrystallisations from benzene gave colourless needles of the *diol* (1·95 g.), m. p. 207—208°, $\nu_{max.}$ (in KBr) 3350, 1036 $cm.^{-1}$ (OH) (Found: C, 80·0; H, 10·3; O, 9·7. $C_{22}H_{34}O_2$ requires C, 79·95; H, 10·4; O, 9·7%). The *di*-p-*nitrobenzoate* was obtained as yellowish prisms, m. p. 197—198°, from methylcyclohexane (Found: C, 68·9; H, 6·3; N, 4·4. $C_{36}H_{40}O_8N_2$ requires C, 68·8; H, 6·4; N, 4·5%). The *diacetate*, colourless needles, had m. p. 145—147° (from ethanol) (Found: C, 74·65; H, 9·2; O, 15·8. $C_{26}H_{38}O_4$ requires C, 75·3; H, 9·2; O, 15·4%).

Removal of methanol from the mother-liquor of the diol and addition of methylcyclohexane gave tiny colourless needles of an isomeric *diol* (1·07 g.), m. p. 177—178° (from benzene), $\nu_{max.}$ (in KBr) 1000, 1015, 3330 $cm.^{-1}$ (OH) (Found: C, 79·7; H, 10·2; O, 9·8%). The *di*-p-*nitrobenzoate* formed colourless prisms, m. p. 183°, from methylcyclohexane (Found: C, 68·9; H, 6·7; N, 4·32%), and the *diacetate* cubes, m. p. 136° (from methanol) (Found: C, 75·2; H, 9·0; O, 15·5%).

Removal of the benzene from the recrystallisation mother-liquors of the diol (VII) and

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chromatography of the residual solid (0·85 g.) in benzene–chloroform (1 : 1; 2 c.c.) over basic alumina (30 g.) afforded, on elution with benzene–chloroform (1 : 1), colourless plates (280 mg.), m. p. 168° (from methylcyclohexane), of the *trans*-ketol (XII). Further elution gave the diol (VII) (510 mg.), m. p. 207° (from benzene).

cis-$\Delta^{16a(16b)}$-*Eicosahydrodicyclo-octa*[a,c]*naphthalene*-7,10-*diol* (VIII).—(*a*) Catalytic reduction at atmospheric pressure of the diol (VII) (0·5 g.) in ethyl acetate (100 ml.) in the presence of Adams catalyst (200 mg.) was complete (88 ml. of hydrogen absorbed) in 50 min. After removal of catalyst and solvent, trituration with methanol gave colourless prisms of the *diol* (VIII) (320 mg.), m. p. 213—214° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3420, 996 cm.$^{-1}$ (OH) (Found: C, 79·4; H, 10·8; O, 9·6. $C_{22}H_{36}O_2$ requires C, 79·5; H, 10·9; O, 9·6%). The *diacetate* formed colourless prisms, m. p. 176—178° (from ethanol) (Found: C, 74·8; H, 9·8; O, 15·5. $C_{26}H_{40}O_4$ requires C, 75·0; H, 9·7; O, 15·4%).

From the mother-liquor of the diol (VIII), the ketol (VI) (100 mg.) was isolated.

(*b*) Reduction of the ketol (VI) (390 mg.) in dry ether (75 ml.) with lithium aluminium hydride (750 mg.) in dry ether (100 ml.), followed by the usual working-up, gave the identical diol (VIII) (320 mg., 82%).

(*c*) Reduction of the diketone (V) (1 g.) in dry ether (50 ml.) with lithium aluminium hydride (1·5 g.) in dry ether (50 ml.) gave the identical diol (VIII) (840 mg., 84%). Identity of the three products was established by mixed m. p. and infrared spectra.

trans-$\Delta^{16a(16b)}$-*Eicosahydrodicyclo-octa*[a,c]*naphthalene*-7(eq),10(eq)-*diol* (X).—The diketone (IX) (1 g.) in dry ether (100 ml.) was added to lithium aluminium hydride (1·5 g.) in dry ether (100 ml.) and boiling was maintained for 6 hr. After the usual working-up, concentration of the ether solution to a small volume gave white needles of the *diol* (X) (650 mg.), m. p. 215—216° (from 2,2,4-trimethylpentane–xylene), $\nu_{max.}$ (in KBr) 3340, 1040 cm.$^{-1}$ (OH) (Found: C, 79·6; H, 10·7; O, 9·5. $C_{22}H_{36}O_2$ requires C, 79·5; H, 10·9; O, 9·6%). The *diacetate* was obtained as colourless needles, m. p. 154—155°, from methanol (Found: C, 74·4; H, 9·6; O, 16·05. $C_{26}H_{40}O_4$ requires C, 75·0; H, 9·7; O, 15·4%).

Removal of the ether from the mother-liquor and trituration with methylcyclohexane gave a colourless solid (156 mg.), m. p. 174° (from methylcyclohexane), identified as the diaxial isomer (XI) (see below).

trans-$\Delta^{6a(16b)}$-*Eicosahydrodicyclo-octa*[a,c]*naphthalene*-7,10-*diol* (XIII).—Reduction of the ketol (XII) (1·4 g.) in dry ether (100 ml.) with lithium aluminium hydride (2·1 g.) in dry ether (100 ml.) afforded, in the usual way, colourless prisms of the *diol* (XIII) (1·2 g., 85%), m. p. 178—180° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3600, 1021, 985 cm.$^{-1}$ (OH) (Found: C, 79·55; H, 11·1; O, 9·7. $C_{22}H_{36}O_2$ requires C, 79·5; H, 10·9; O, 9·6%). The *diacetate*, needles, had m. p. 178—180° (from ethanol) (Found: C, 74·6; H, 9·5; O, 15·9. $C_{26}H_{40}O_4$ requires C, 75·0; H, 9·7; O, 15·4%).

trans-$\Delta^{16a(16b)}$-*Eicosahydrodicyclo-octa*[a,c]*naphthalene*-7(ax),10(ax)-*diol* (XI).—Sodium borohydride (0·7 g.) was added portionwise to a solution of the diketone (IX) (0·7 g.) in methanol (100 ml.) and the mixture left overnight. After the usual working-up the *diol* (XI) (600 mg., 85%) was obtained as colourless prisms, m. p. 174° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3510, 1030 cm.$^{-1}$ (OH) (Found: C, 79·7; H, 10·7; O, 9·6%). Admixture of all possible combinations of (XI), (XIII), and the unidentified isomer of (VII) gave depressions in m. p.

The rhombohedral *diacetate* of compound (XI) had m. p. 105° (from methanol) (Found: C, 74·6; H, 9·6; O, 16·0%).

A portion of the crude reduction product (300 mg.) in benzene–chloroform was chromatographed over acid-washed alumina (15 g.). Elution with benzene–hexane (1 : 1) changing to pure benzene afforded the diol (XI) (207 mg.). Further elution with benzene–chloroform (1 : 1) gave a crude mixture (31 mg.), m. p. 177—185°. Elution with pure chloroform finally gave the isomeric diol (X) (43 mg.).

Saponification of Diacetates of (X) *and* (XI).—A sample of each diacetate (30 mg.) was dissolved in neutral dioxan (3 ml.) and the solution was made up to 10 ml. with 0·1N-sodium hydroxide. Aliquot parts (1 ml.) were titrated at different times with 0·01N-hydrochloric acid at 25·6°, with the results tabulated.

	% Hydrolysed						
Time (min.)	300	570	1350	1770	2760	3210	4230
Diacetate from (X)	10·8	29·0	60·8	65·4	77·8	79·7	84·3
,, ,, (XI)	6·1	16·8	47·2	53·5	67·9	71·2	75·3

Oxidation of Diols (X) *and* (XI).—A sample of each diol (0·991 mg.) was dissolved in acetic acid (9 ml.) and oxidised at 20° c with chromic acid (0·800 mg.) in water (1 ml.). We are grateful to Drs. Schreiber and Eschenmoser of E.T.H., Zürich, for the following data: (X), *k'* 6·3, $t_{1/2}$ 20 min.; (XI) *k'* 9·4, $t_{1/2}$ 16 min.

Oxidation of Diols.—(*a*) A solution of diol (VII) (0·5 g.) in pyridine (5 ml.) was added to the chromium trioxide–pyridine complex (from 1 g. and 10 ml. respectively). After 24 hr. at room temperature, benzene (20 ml.) was added and the precipitate was removed. An equal volume of ether was added to the filtrate. After washing with dilute hydrochloric acid containing 5% aqueous ferrous sulphate, drying (Na_2SO_4), and removal of solvents, trituration with methanol gave a brown solid (120 mg.), m. p. 104° (from ethanol), identical (mixed m. p.) with the diketone (II). Similar oxidation of the diol, m. p. 177—178°, isomeric with (VII), also gave diketone (II).

(*b*) A solution of the diol (VII) (1·8 g.) in acetic acid (80 ml.) and benzene (20 ml.) was added during 1 hr. to a cooled solution of chromic acid (1·8 g.) in 80% acetic acid (20 ml.) at 5° and left overnight. After the usual working-up and extraction of the oily product three times with boiling hexane, removal of the solvent from this extract and trituration with methanol gave yellow needles (120 mg.), m. p. 152° (from ethanol), identical (mixed m. p.) with the quinone (III). Similar oxidation of the isomeric diol, m. p. 177—178°, gave the same quinone (III).

The following Table summarises analogous oxidations of other diols:

		Oxidant		
Diol	Solvent	CrO_3	C_5H_5N	Products
VIII; 0·5 g.	C_5H_5N; 10 ml.	1 g.	10 ml.	V; 10 mg., 2% VI; 10 mg., 2%
VI; 0·16 g.	C_5H_5N; 5 ml.	0·3 g.	5 ml.	V; 50 mg., 31%
XI; 0·5 g.	C_5H_5N; 10 ml.	1 g.	10 ml.	IX; 100 mg., 20%
X; 0·6 g.	AcOH; 100 mml.	0·6	(80% AcOH; 10 ml.)	IX; 10 mg., 2%

trans-$\Delta^{6a(16b)}$-*Eicosahydrodicycloheptа*[a,c]*naphthalene*-7,10-*dione* (XIV).—Oxidation of the diol (XIII) (0·25 g.) in pyridine (5 ml.) with the pyridine (5 ml.)–chromic acid (0·5 g.) complex as described above gave a yellowish oil. Trituration with methanol afforded white needles of the *diketone* (XIV) (110 mg., 21%), m. p. 124—125° (from methanol; carbon), $\nu_{max.}$ (in $CHCl_3$) 1710 cm.$^{-1}$ (saturated C=O), $\lambda_{max.}$ (in dioxan) 244 mμ (log ε 3·26) (Found: C, 80·3; H, 9·5; O, 9·9. $C_{22}H_{32}O_2$ requires C, 80·4; H, 9·8; O, 9·7%).

The identical diketone (XIV) was obtained by oxidising the ketol (XII) (0·25 g.) in pyridine (5 ml.) with the same reagent.

Diketone (IX) *from its Isomer* (XIV).—Refluxing the $\Delta^{6a(16b)}$-diketone (XIV) (0·4 g.) in benzene (50 ml.) with naphthalene-β-sulphonic acid (0·3 g.) for 2 hr. and washing the cooled solution with aqueous sodium hydrogen carbonate was followed by drying ($MgSO_4$) and removal of the solvent. Trituration with methanol gave white needles (350 mg., 88%), m. p. 145° (from hexane), identical with the *trans*-$\Delta^{16a(16b)}$-diketone (IX) (mixed m. p. and infrared spectra).

1,2,3,4,5,6,6a,6b,11,12,13,14,15,16-*Tetradecahydrodicyclo-octа*[a,c]*naphthalene* (XV).—The diol (VII) (2 g.) was stirred during 4 hr. with 85% phosphoric acid (2 g.) at 100°. Dilution with water, extraction with ether, washing the ether layer with aqueous sodium hydrogen carbonate and water, drying (Na_2SO_4), and removal of the ether gave an oil. Trituration with methylcyclohexane gave solid starting material. Evaporation of the filtrate and addition of 2,2,4-trimethylpentane to the residue gave the colourless ketol (VI) (130 mg.). Concentration of the filtrate therefrom to a small volume and cooling at −10° for a week gave cubes, m. p. 56—57° (from 2,2,4-trimethylpentane). Cooling the mother-liquor at 5° gave another crop of the *hydrocarbon* (XV) (total 0·7 g., 39%), $\lambda_{max.}$ (in cyclohexane [12]) 241, 265, 272, 297 mμ (log ε 4·99, 3·94, 3·97, 3·79) (Found: C, 90·0; H, 10·4. $C_{22}H_{30}$ requires C, 89·7; H, 10·3%).

1,2,3,4,5,6,11,12,13,14,15,16-*Dodecahydrodicyclo-octа*[a,c]*naphthalene* (XVI).—The hydrocarbon (XV) (1 g.) was dehydrogenated in acetic acid (10 ml.) with *p*-benzoquinone (2 g.) at 100° for 8 hr. The black precipitate was removed from the cooled solution and washed with cold methanol, leaving white needles (0·7 g.). Removal of the acetic acid from the filtrate, followed by the usual working-up, gave another crop of the *hydrocarbon* (XVI) (total 0·82 g., 83%), m. p. 139° (from acetic acid), $\lambda_{max.}$ (in cyclohexane [13]) 238, 287, 297 mμ (log ε 4·99, 3·76, 3·81) (Found: C, 90·2; H, 9·5. $C_{22}H_{28}$ requires C, 90·35; H, 9·65%).

[12] Cf. Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, 1951, No. 129.

[13] Cf. ref. 12, no. 195.

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7,10 - *Diacetoxy* - 1,2,3,4,5,6,11,12,13,14,15,16 - *dodecahydrodicyclo* - *octa*[a,c]*naphthalene* (XVIII).—The diacetate (XVII) (0·5 g.) was dehydrogenated by heating it with 30% palladised carbon (200 mg.) at 220—240° for 2 hr. Benzene was added and the catalyst removed by filtration. Removal of benzene at the water-pump and trituration of the residue with hexane gave the yellowish *dodecahydro-diacetate* (XVIII) (200 mg.) as prisms, m. p. 230° (from acetic acid), $\lambda_{max.}$ (in dioxan) 244, 310 mμ (log ε 4·80, 3·93) (Found: C, 76·4; H, 7·9; O, 15·5. $C_{36}H_{52}O_4$ requires C, 76·4; H, 7·9; O, 15·7%).

1,2,3,4,5,6,7,8,9,10,11,12,12a,12b,13,13b,14,15,16,17,18,19,20,21,22,23,24,25,25a,26,26a,26b-*Dotriacontahydrotetracyclo-octa*[a,c,h,j]*anthracene*-13,26-*dione* (XIX).—The diketone (II) (0·5 g., 0·0015 mole) was heated with bicyclo-oct-1-enyl (0·66 g., 0·003 mole) for 30 min. at 100°. A pentane solution of the yellow oily product deposited during 12 hr. at room temperature a yellowish amorphous solid (0·5 g.). The analytical sample of this *diketone* (XIX) formed yellowish prisms, m. p. 197° (from butan-1-ol), $\nu_{max.}$ (in $CHCl_3$) 1680 cm.$^{-1}$ (C=C·C=O) (Found: C, 84·3; H, 9·7; O, 6·0. $C_{38}H_{54}O_2$ requires C, 84·1; H, 10·0; O, 5·9%).

1,2,3,4,5,6,7,8,9,10,11,12,12a,12b,13,14,15,16,17,18,19,20,21,22,23,24,25,26,26a,26b-*Triacontahydrotetracyclo-octa*[a,c,h,j]*anthracene*-13,26-*dione* (XX).—A solution of the diketone (III) (0·5 g., 0·0015 mole) in bicyclo-oct-1-enyl (0·66 g., 0·003 mole) was heated at 100° for 10 min. Trituration with pentane gave a solid (0·88 g.), yielding large yellowish prisms of the *diketone* (XX) (0·8 g.), m. p. 213° (from acetic acid), $\nu_{max.}$ (in $CHCl_3$) 1670 cm.$^{-1}$ (C=C·C=O), $\lambda_{max.}$ (in dioxan) 240μ (log mε 4·43) (Found: C, 84·5; H, 9·6; O, 6·1. $C_{38}H_{52}O_2$ requires C, 84·4; H, 9·7; O, 5·9%).

1,2,3,4,5,6,7,12,13,14,15,16-*Dodecahydrodicyclo-octa*[a,c]*anthracene*-7,12-*dione* (XXI).—1,2,3,4,5,6,6a,6b,7,12,12a,12b,13,14,15,16-Hexadecahydrodicyclo-octa[*a,c*]anthracene-7,12dione-(0·5 g.) was dehydrogenated by *p*-benzoquinone (2 g.) in acetic acid (20 ml.) at 100° for 4 hr. Another portion of benzoquinone (2 g.) was then added and heating continued for 4 hr. The usual working-up gave the *diketone* as yellow needles (200 mg., 40%), m. p. 164° (from acetic acid), $\nu_{max.}$ (in $CHCl_3$) 1665 cm.$^{-1}$ (quinonoid C=O), $\lambda_{max.}$ (in dioxan) 269, 358 mμ (log ε 4·65, 3·82) (Found: C, 84·0; H, 7·7; O, 8·4. $C_{26}H_{28}O_2$ requires C, 83·3; H, 7·6; O, 8·6%).

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295. *Alicyclic Studies. Part XVII.* Preparation and Reactions of Bicyclodec-1-enyl.*

By Jacob Strumza and David Ginsburg.

Bicyclodec-1-enyl has been prepared by dehydration of bicyclodecyl-1,1′-diol. Diels–Alder reactions of this new diene with a number of dienophiles are described.

Cyclodecanone was reduced to the pinacol, bicyclodecyl-1,1′-diol with aluminium amalgam in dry benzene. A very small amount of self-condensation of cyclodecanone occurs during the reduction, leading to the formation of 2-cyclodecylidenecyclodecanone. The latter through 1,4-reduction with lithium aluminium hydride gave 2-cyclodecylcyclodecanol.

The pinacol was dehydrated by our improved procedure with phosphorus oxychloride in pyridine.[1] We had hoped that we might isolate several geometrical isomers of the diene but the steric course of the elimination appears to be unique as the resulting bicyclodec-1-enyl was easily obtained crystalline. Unfortunately, however, its infrared spectrum does not show clear bands for either *cis*- or *trans*-double bonds.

The diene gave adducts in high yields with maleic anhydride, *p*-benzoquinone, and 1,4-naphthaquinone (see Experimental section). Conditions could not be discovered to

* Part XVI, Strumza and Ginsburg, preceding paper.

[1] Greidinger and Ginsburg, *J. Org. Chem.*, 1957, **22**, 1406.

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shift the equilibrium with dimethyl acetylenedicarboxylate in the direction of the adduct. Further transformations of the maleic anhydride adduct will be reported in the following paper in connexion with analogous adducts of bicyclohex-1-enyl and bicyclo-oct-1-enyl.[2]

Experimental

Bicyclodecyl-1,1′-diol.—A mixture of coarse aluminium powder (14·4 g.) and mercuric chloride (10·8 g.) was added to a stirred solution of cyclodecanone [3] (40 g.) in dry benzene (80 ml.). The resulting exothermic reaction caused the solvent to reflux gently. The mixture was heated under reflux with stirring overnight. Wet benzene (60 ml.) was added, followed by water (60 ml.) with stirring. After 30 minutes' heating the solid was removed and was extracted twice with boiling benzene. The benzene from the combined extracts was removed at the water-pump. Distillation gave unchanged ketone, b. p. 126—128°/26 mm. (5·7 g.). A pentane solution of the residual oil afforded after 12 hr. at 5° colourless prisms (15·8 g., 55%) of the *pinacol*, m. p. 106° (from 2,2,4-trimethylpentane), $\nu_{max.}$ (in $CHCl_3$) 3550 cm.$^{-1}$ (OH) (Found: C, 77·25; H, 12·4; O, 10·5. $C_{20}H_{38}O_2$ requires C, 77·4; H, 12·3; O, 10·3%).

Distillation afforded more cyclodecanone (5·6 g.). The residual oil was dissolved in ethanol; in 12 hr. at 5° the solution deposited colourless needles (830 mg.) of a dimer assumed to be *2-cyclodecylidenecyclodecanone*, m. p. 81° (from ethanol), $\nu_{max.}$ (in $CHCl_3$) 1695 cm.$^{-1}$ (–C=C·C=O), $\lambda_{max.}$ (in dioxan) 300 mμ (log ε 1·51) (Found: C, 81·9; H, 12·4; O, 5·9. $C_{20}H_{34}O$ requires C, 82·7; H, 11·8; O, 5·5%).

Reduction of this ketone with lithium aluminium hydride in ether gave *2-cyclodecylcyclodecanol* as colourless prisms, m. p. 81—82° (from ethanol), $\nu_{max.}$ (in $CHCl_3$) 3630 cm.$^{-1}$ (OH) (Found: C, 81·2; H, 13·3; O, 5·6. $C_{20}H_{38}O$ requires C, 81·6; H, 13·0; O, 5·4%).

Bicyclodec-1-enyl.—A solution of the pinacol (20 g.) in dry pyridine (400 ml.) was heated under reflux with phosphorus oxychloride (20 ml.) for 2 hr. Most of the pyridine was removed at the water-pump and water (10 ml.) was shaken with the ice-cold residue for 30 min. Extraction with pentane (3 × 300 ml.), washing with dilute hydrochloric acid and with water, drying ($MgSO_4$), and removal of the pentane, gave the oily *diene* (12·5 g., 71%) that crystallised as rhombs, m. p. 64—65°, from propan-2-ol. It had $\lambda_{max.}$ (in methylcyclohexane) 235 mμ (log ε 4·06) but in $CHCl_3$ did not show infrared bands of either a *cis*- or a *trans*-double bond (Found: C, 87·45; H, 12·4. $C_{20}H_{34}$ requires C, 87·5; H, 12·5%).

1,2,3,4,5,6,7,8,8a,9,10,10a,11,12,13,14,15,16,17,18-*Eicosahydrodicyclodeca*[a,c]*benzene*-9,10-*dicarboxylic Anhydride.*—A solution of bicyclodec-1-enyl (5 g.) and maleic anhydride (2·7 g.) in xylene (15 ml.) was heated under reflux for 3 hr. The cooled mixture solidified and gave white needles of the *anhydride* (5·45 g., 80%), m. p. 184° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 1845, 1775 cm.$^{-1}$ (C=O of anhydride) (Found: C, 77·3; H, 9·8; O, 12·9. $C_{24}H_{36}O_3$ requires C, 77·4; H, 9·7; O, 12·9%).

Aromatisation of the six-membered ring was effected by refluxing the adduct (0·74 g., 0·002 mole) in chloroform (50 ml.) with bromine (0·32 g., 0·004 mole) for 5 hr. After washing of the solution with 5% sodium hydrogen carbonate solution and with water, the chloroform was removed. Trituration of the residue with methanol gave colourless needles of the aromatic *anhydride* (80 mg., 11%), m. p. 191° (from acetic acid), $\nu_{max.}$ (in $CHCl_3$) 1835, 1765 cm.$^{-1}$ (C=O of anhydride) (Found: C, 78·0; H, 8·8; O, 13·1. $C_{24}H_{32}O_3$ requires C, 78·2; H, 8·75; O, 13·0%).

1,2,3,4,5,6,7,8,8a,8b,9,10,11,12,13,14,14a,14b,15,16,17,18,19,20,21,22-*Hexacosahydrodicyclodeca*[a,c]*anthracene*-9,14-*dione.*—A nitrobenzene (20 ml.) solution of bicyclodec-1-enyl (2·19 g., 0·008 mole) and 1,4-naphthaquinone (1·26 g., 0·008 mole) was heated at 150° for 3 hr. Steam-distillation to remove nitrobenzene was followed by extraction of the dark residue with chloroform. Removal of the chloroform and extraction with hexane, removal of the solid by filtration and of the hexane from the mother-liquor gave an oil which upon trituration with propan-2-ol gave slender yellow needles (1·24 g., 36%) of the *diketone*, m. p. 141° (from propan-2-ol), $\nu_{max.}$ (in $CHCl_3$) 1660 cm.$^{-1}$ (C=O conjugated to aromatic nucleus), $\lambda_{max.}$ (in dioxan) 247, 277, 337 mμ (log ε 4·24, 4·10, 3·47) (Found: C, 83·6; H, 9·1; O, 6·8. $C_{30}H_{40}O_2$ requires C, 83·3; H, 9·3; O, 7·4%).

[2] Strumza and Ginsburg, following paper.
[3] Cope, *Org. Synth.*, 1956, **36**, 79.

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Dehydrogenation of this diketone (0·5 g.) was effected in acetic acid (20 ml.) with *p*-benzoquinone (2 g.) at 100° for 4 hr. *p*-Benzoquinone (2 g.) was again added and heating prolonged for another 4 hr. The black precipitate was removed from the ice-cold mixture and washed with cold methanol. The *docosahydro-diketone* (350 mg., 59%) was obtained as yellow needles, m. p. 218° (from dioxan), $\nu_{max.}$ (in $CHCl_3$) 1655 cm.$^{-1}$ (quinonoid C=O), $\lambda_{max.}$ (in dioxan) [4] 241, 269, 361 mμ (log ε 4·54, 4·60, 3·65) (Found: C, 84·2; H, 8·4; O, 7·6. $C_{30}H_{36}O_2$ requires C, 84·1; H, 8·5; O, 7·5%).

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[4] Cf. Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, 1951, No. 395.

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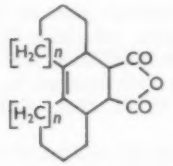
296. *Alicyclic Studies. Part XVIII.* Homologous Cyclic Lactone-acids.*

By Jacob Strumza and David Ginsburg.

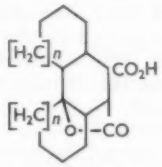
The formation of lactone-acids of type (II) and various reactions of these compounds are described.

When the Diels–Alder adduct (Ic) of bicyclodec-1-enyl and maleic anhydride was saponified under acidic conditions a lactone-acid (IIc) was obtained. This type of lactonisation has been reported for other systems.[1]

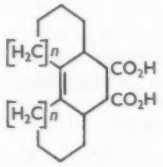
Since the six- and eight-membered ring homologues were more readily available we studied their analogous behaviour. Bicyclohex-1-enyl [2] and bicyclo-oct-1-enyl [3] gave with maleic anhydride the corresponding anhydrides (Ia and b). Both anhydrides afforded lactone-acids (IIa and b) on saponification in acid medium. Alkaline saponification of the anhydrides (Ia and b) permitted isolation of the unlactonised dicarboxylic acids (IIIa and b).



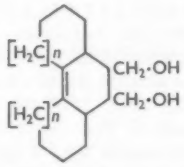
(I) a: $n = 1$
b: $n = 3$
c: $n = 5$



(II) a: $n = 1$
b: $n = 3$
c: $n = 5$



(III) a: $n = 1$
b: $n = 3$



(IV) a: $n = 1$
b: $n = 3$
c: $n = 5$

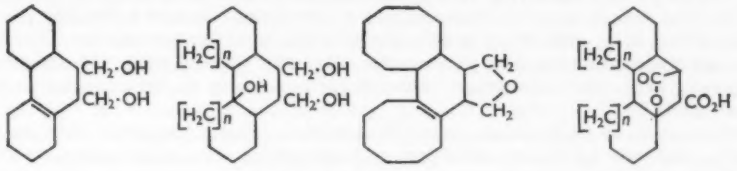
Reduction of the anhydride (Ic) with lithium aluminium hydride gave a diol (IVc). Similar diols (IVa and b) were obtained by reducing the diacid (IIIa) or the anhydride (Ib) with lithium aluminium hydride. The same reagent converted the lactone-acids (IIa and b) into the triols (VIa and b).

Dehydration of the triol (VIa) gave a diol (V), isomeric with (IVa), in which the double bond is presumed to be in the 4a,10a-position, by analogy with the behaviour of condensed six-membered alicyclic systems.

* Part XVII, preceding paper.

[1] Mousseron and Mousseron-Canet, *Compt. rend.*, 1957, **245**, 2156; Mousseron, Mousseron-Canet, and Graner, Colloque Internat. Stereochimie, Montpellier, Septembre, 1959; Klein, *J. Org. Chem.*, 1958, **23**, 1209; Barton and Holness, *J.*, 1952, 78.
[2] Gruber and Adams, *J. Amer. Chem. Soc.*, 1935, **57**, 2555.
[3] Greidinger and Ginsburg, *J. Org. Chem.*, 1957, **22**, 1406.

It is believed that an analogous shift of the double bond may occur during acidic dehydration of the triol (VIb). This would lead to a cyclic ether (VII) identical with the



(V) (VI) a: $n = 1$ b: $n = 3$ (VII) (VIII)

product of acidic dehydration of the diol (IVb) in which the double bond also rearranges from the position exocyclic with respect to the two eight-membered rings to a position inside one of them (also inside the six-membered ring).[4]

It must be noted that although the structures (II) have been formulated as shown above, an alternative structure (VIII) has not been ruled out unequivocally. The products obtained from the lactone (II) by various interconversions could also be explained on the basis of (VIII), and a study of Dreiding models does not show an appreciable difference in steric interactions in the two formulations.

Experimental

10,18a-*Lactone* (IIc) *of Perhydro*-18a-*hydroxydicyclodeca*[a,c]*benzene*-9,10-*dicarboxylic Acid*.—A solution of the anhydride [5] (Ic) (1 g.) in 95% acetic acid (30 ml.) and concentrated hydrochloric acid (10 ml.) was heated under reflux for 5 hr. and left overnight. The solution was then poured into ice-water and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogen carbonate and water. Drying ($MgSO_4$), removal of the ether, and trituration with ethanol gave the *lactone-acid* (240 mg.) as colourless prisms, m. p. 249° (from methanol), $\nu_{max.}$ (in KBr) 1770 (γ-lactone), 1710 cm.$^{-1}$ (CO_2H) (Found: C, 73·8; H, 9·7; O, 16·5%; equiv., 391. $C_{24}H_{38}O_4$ requires C, 73·8; H, 9·8; O, 16·4%; equiv., 391).

$\Delta^{18a(18b)}$*Eicosahydro*-9,10-*di*(*hydroxymethyl*)*dicyclodeca*[a,c]*benzene* (IVc).—Reduction of the anhydride (Ic) (1·5 g.) with lithium aluminium hydride (3 g.) in dry ether (500 ml.) gave, after the usual working-up, the *diol* (IVc) (1·4 g., 96%) as colourless prisms, m. p. 155° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3650 cm.$^{-1}$ (OH) (Found: C, 79·6; H, 11·6; O, 9·0. $C_{24}H_{42}O_2$ requires C, 79·5; H, 11·7; O, 8·8%).

$\Delta^{4a(4b)}$*Dodecahydrophenanthrene*-9,10-*dicarboxylic Acid* (IIIa).—A solution of the anhydride [5] (Ia) (1 g.) in ethanol (84 ml.) and 30% aqueous potassium hydroxide (16 ml.) was heated under reflux for 1 hr. Most of the ethanol was removed at the water-pump, and saturated salt solution (50 ml.) added. After acidification with dilute hydrochloric acid and ether-extraction, the extract was dried ($MgSO_4$) and the solvent was removed. Trituration with hexane gave colourless prisms of the *diacid* (700 mg., 66%), m. p. 206° (decomp.) (from acetic acid), $\nu_{max.}$ (in KBr) 1710 cm.$^{-1}$ (CO_2H) (Found: C, 68·6; H, 7·7; O, 23·8. $C_{16}H_{22}O_4$ requires C, 69·0; H, 8·0; O, 23·0%).

The *dimethyl ester*, obtained by treatment with diazomethane in ether, formed colourless prisms, m. p. 109° (from 2,2,4-trimethylpentane), $\nu_{max.}$ (in $CHCl_3$) 1740 cm.$^{-1}$ (ester C=O) (Found: C, 70·6; H, 8·6; O, 20·85. $C_{18}H_{26}O_4$ requires C, 70·6; H, 8·55; O, 20·9%).

10,4a-*Lactone of* 4a-*Hydroxyperhydrophenanthrene*-9,10-*dicarboxylic Acid* (IIa).—A solution of the anhydride (Ia) (5 g.) in 95% acetic acid (100 ml.) and concentrated hydrochloric acid (33 ml.) was heated under reflux for 5 hr. After the working-up described for (Ic), the *lactone-acid* was obtained as slender colourless needles (3·5 g., 69%), m. p. 247—248° (from xylene), $\nu_{max.}$ (in KBr) 1780 (γ-lactone), 1690 cm.$^{-1}$ (CO_2H) (Found: C, 69·0; H, 8·3; O, 22·7%; equiv., 278·5. $C_{16}H_{22}O_4$ requires C, 69·0; H, 8·0; O, 23·0%; equiv., 278·3).

[4] Cf. Cope, Ambros, Ciganek, Howell, and Jacura, *J. Amer. Chem. Soc.*, 1959, **81**, 3153.
[5] Strumza and Ginsburg, preceding paper.

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The *methyl ester* obtained by treatment with ethereal diazomethane formed plates, m. p. 140° (from aqueous methanol) (Found: C, 69·8; H, 8·4; O, 21·75. $C_{17}H_{24}O_4$ requires C, 69·8; H, 8·3; O, 21·8%), $\nu_{max.}$ (in $CHCl_3$) 1770 (γ-lactone), 1730 cm.$^{-1}$ (ester C=O).

The identical (mixed m. p.) lactone-acid (0·9 g., 45%) was obtained by heating the dicarboxylic acid (IIIa), m. p. 206° (2 g.), in 98% formic acid (40 ml.) at 80° for 2 hr. Pouring into ice-water and ether-extraction, etc., gave needles, m. p. 247° (from xylene). It is possible that the compound, m. p. 242°, described [3] as the diacid is actually the lactone-acid, m. p. 247° in impure form.

$\Delta^{4a(4b)}$*Dodecahydro-9,10-di(hydroxymethyl)phenanthrene* (IVa).—Reduction of the diacid (IIIa), m. p. 206° (800 mg.), in dry ether (250 ml.) with lithium aluminium hydride (2 g.) in dry ether (200 ml.) gave the *dialcohol* (400 mg., 64%) as colourless prisms, m. p. 136—137° (from methylcyclohexane), $\nu_{max.}$ (in KBr) 3250 cm.$^{-1}$ (OH) (Found: C, 76·8; H, 10·45; O, 12·7. $C_{16}H_{26}O_2$ requires C, 76·75; H, 10·5; O, 12·8%). The same dialcohol (1·3 g.) was obtained by reducing the anhydride (Ia) (2 g.) in dry ether (250 ml.) with lithium aluminium hydride (4 g.) in dry ether (250 ml.).

Perhydro-9,10-di(hydroxymethyl)phenanthren-4a-ol (VIa).—Reduction of the lactone-acid (IIa) (2 g.) in dry ether (300 ml.) with lithium aluminium hydride (4 g.) in dry ether (200 ml.) gave the *triol* as colourless rhombs (1 g., 52%), m. p. 200° (from ethanol), $\nu_{max.}$ (in KBr) 3180 cm.$^{-1}$ (broad; OH) (Found: C, 71·6; H, 10·6; O, 18·1. $C_{16}H_{28}O_3$ requires C, 71·6; H, 10·5; O, 17·9%).

The *diacetate* formed colourless platelets, m. p. 112° (from methanol), $\nu_{max.}$ (in $CHCl_3$) 3600 (OH), 1725 cm.$^{-1}$ (ester C=O) (Found: C, 68·3; H, 9·15; O, 22·5. $C_{20}H_{32}O_5$ requires C, 68·15; H, 9·15; O, 22·7%).

When the triol (0·5 g.) was heated under reflux with dry benzene (100 ml.) in the presence of naphthalene-β-sulphonic acid (0·25 g.) for 5 hr., dehydration occurred with migration of the double bond. Concentration of the neutralised benzene solution gave plates (0·3 g., 64%) of a *diol* (V) believed to be the $\Delta^{4a(10a)}$-isomer. It had m. p. 153° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3640 cm.$^{-1}$ (OH) (Found: C, 76·3; H, 10·4; O, 13·5. $C_{16}H_{26}O_2$ requires C, 76·75; H, 10·5; O, 12·8%).

The diol (IV) rearranged to this diol (V) when heated with naphthalene-β-sulphonic acid in benzene.

8,14a-*Lactone* (IIb) *of* $\Delta^{14a(14b)}$*-Octadecahydro-14a-hydroxydicyclo-octa*[a,c]*benzene-7,8-dicarboxylic Acid*.—The anhydride (Ib) (4 g.) was dissolved in 95% acetic acid (120 ml.) containing concentrated hydrochloric acid (5 ml.) and refluxing was maintained for 3 hr. The solvent was removed at the water-pump and the residue was triturated with benzene (100 ml.). The cooled solution deposited needles of the *lactone-acid* (950 mg.), m. p. 274° (decomp.) (from ethanol), $\nu_{max.}$ (in KBr) 1770 (γ-lactone), 1708 cm.$^{-1}$ (CO_2H) (Found: C, 71·5; O, 19·1; H, 9·3%); equiv., 335·0. $C_{20}H_{34}O_4$ requires C, 71·8; H, 9·0; O, 19·1%; equiv., 334·4). Concentration of the benzene solution gave starting material (3 g.).

The *methyl ester*, obtained (82%) by Fischer esterification, formed colourless cubes, m. p. 137° (from 2,2,4-trimethylpentane), $\nu_{max.}$ (in $CHCl_3$) 1770 (γ-lactone), 1730 cm.$^{-1}$ (ester) (Found: C, 72·2; H, 9·3; O, 18·3. $C_{21}H_{32}O_4$ requires C, 72·4; H, 9·3; O, 18·4%).

$\Delta^{14a(14b)}$*-Hexadecahydrodicyclo-octa*[a,c]*benzene-7,8-dicarboxylic Acid* (IIIb.)—A solution of the anhydride (Ib) (2 g.) in ethanol (10 ml.) and 30% aqueous potassium hydroxide (30 ml.) was heated under reflux for 1 hr. Most of the ethanol was removed at the water-pump, and the basic solution was diluted with water (30 ml.). The potassium salt of the diacid was separated by filtration, purified by crystallisation from ethanol (3·9 g., 75%), and dried by washing with ether. It was then dissolved in ice-water (50 ml.) and shaken with ether (100 ml.) and dilute hydrochloric acid (10 ml.). The aqueous layer was extracted with ether, the combined ether extracts were washed with water, dried ($MgSO_4$), and the solvent was removed at 40°. Trituration of the oily residue with pentane gave the diacid as a colourless amorphous solid (2 g., 48%), m. p. 178—180° with formation of the anhydride, $\nu_{max.}$ (in KBr) 1710 cm.$^{-1}$ (CO_2H).

The *dimethyl ester*, prepared with diazomethane in cold ether, formed prisms, m. p. 97° (from pentane), $\nu_{max.}$ (in $CHCl_3$) 1740 cm.$^{-1}$ (ester C=O) (Found: C, 72·65; H, 9·4; O, 17·5. $C_{22}H_{34}O_4$ requires C, 72·9; H, 9·45; O, 17·7%).

Perhydro-14a-hydroxy-7,8-di(hydroxymethyl)dicyclo-octa[a,c]*benzene* (VIb).—Reduction of the lactone-ester, m. p. 137° (1·4 g.), in dry ether (100 ml.) with lithium aluminium hydride (2 g.)

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in dry ether (100 ml.) gave the *triol* (VIb) (1·2 g., 91%) as colourless rhombs, m. p. 117° (from benzene), $\nu_{max.}$ (in $CHCl_3$) 3650 cm.$^{-1}$ (OH) (Found: C, 74·1; H, 11·1; O, 14·9. $C_{39}H_{36}O_3$ requires C, 74·0; H, 11·2; O, 14·8%).

$\Delta^{14a(14b)}$-*Hexadecahydro-7,8-di(hydroxymethyl)dicyclo-octa*[a,c]*benzene* (IVb).—Reduction of the anhydride (Ib) (2·7 g.) in dry ether (200 ml.) with lithium aluminium hydride (5·4 g.) in dry ether (250 ml.) gave, in the usual way, colourless prisms of the *diol* (IVb) (1·6 g., 61%), m. p. 128—130° (from methylcyclohexane), $\nu_{max.}$ (in $CHCl_3$) 3330 cm.$^{-1}$ (OH) (Found: C, 78·6; H, 10·85; O, 10·7. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·2; O, 10·4%).

$\Delta^{3b(9a)}$-*Hexadecahydrodicyclo-octa*[e,g]*isobenzofuran* (VII).—The diol (IVb) (0·5 g.) was heated under reflux in benzene (50 ml.) containing naphthalene-β-sulphonic acid (0·3 g.) for 2 hr. The usual working-up gave prisms (160 mg.) of the cyclic *ether* (VII), m. p. 190° (from methanol) (Found: C, 83·1; H, 11·0; O, 5·6. $C_{20}H_{32}O$ requires C, 83·3; H, 11·2; O, 5·55%).

The identical ether (70 mg.) was obtained by dehydration of the triol (VIb) (200 mg.) with naphthalene-β-sulphonic acid (200 mg.) in boiling benzene during 2 hr.

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297. *The Kinetics of the Hydrolysis of t-Butyl Chloride.*

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The kinetics of the hydrolysis of t-butyl chloride in water has been measured conductimetrically. A drift in the apparent unimolecular constant has been quantitatively related to the interionic electrolyte effect, and the rate of chemical change is found to be strictly unimolecular over the complete reaction. Unimolecular constants at 0° and 25° are in reasonable agreement with those measured potentiometrically by Winstein and Fainberg. Those measured at intervening temperatures show that the energy of activation decreases as the temperature is raised. Hydroxyl ions have no effect on the rate, in agreement with the original observation by Hughes on the solvolysis of t-butyl chloride in mixed solvents.

The mechanisms of hydrolysis and substitution at a saturated carbon atom are briefly discussed in terms of hypotheses advanced in earlier papers of this series and in terms of the theory of Hughes and Ingold with which they are not in conflict.

THE work described here was undertaken in order to compare the velocity and energy of activation of the hydrolysis of butyl chloride with the corresponding values for other alkyl halides,[1] particularly methyl chloride.[2] Although numerous papers have been published on the rates of reaction of t-butyl chloride with mixed solvents containing water,[3] only one attempt appears to have been made [4] to study the kinetics of its hydrolysis in water alone. The present results, obtained by the method of electrical conductivity, confirm and extend those obtained potentiometrically.

EXPERIMENTAL

Materials and Method.—(1) Purchased t-butyl chloride, proving to be grossly impure, was fractionally distilled, and the sample boiling at 50·5° retained. This was redistilled from anhydrous sodium sulphate, and the middle fraction (b. p. 50·3—50·4°) was used. It had n_D^{20} 1·38411; Timmermans [5] gives n_{Hg}^{15} 1·38557.

(2) The Pyrex conductivity cells held 30—300 c.c., but in each the electrodes were at a

[1] Moelwyn-Hughes, *J.*, 1933, 1576.
[2] Moelwyn-Hughes, *Proc. Roy. Soc.*, 1938, *A*, **164**, 295; 1953, *A*, **220**, 386; Heppolette and Robertson, *ibid.*, 1959, *A*, **252**, 273; and papers cited in Moelwyn-Hughes, "Kinetics of Reactions in Solution," Oxford, 1947.
[3] E. D. Hughes, *J.*, 1935, 255, and other papers cited by Ingold in "Structure and Mechanism in Organic Chemistry," Bell, London, 1953; Olson and Halford, *J. Amer. Chem. Soc.*, 1937, **59**, 2644.
[4] Winstein and Fainberg, *J. Amer. Chem. Soc.*, 1957, **79**, 5937.
[5] Timmermans, "Physicochemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950.

distance of 10 cm. apart. The neck of each cell was in the middle, and ended in a ground-glass stopper fitted with a mercury cup. The cell and a variable resistance in a 5-decade resistance box reading from 10^{-2} to 10^{5} ohms were balanced in a circuit which included a Wien bridge R.C. oscillator tuned to 1000 cycles per second and a detector capable of dealing with a wide range of signal intensity. Cell constants, C, were determined by using 0·10043m-potassium chloride [6] of specific conductivity of 0·028849 ohm^{-1} $cm.^{-1}$ at 25°. Most of the runs were carried out in four cells, for which the C values were 0·9767, 2·679, 3·452, and 5·219 $cm.^{-1}$.

(3) In a typical run, conductivity water (~50 c.c.) was degassed and placed in a 100 c.c. glass-stoppered conical flask in the thermostat bath. After the water had reached a steady temperature, t-butyl chloride (about 0·05 c.c.) was added from a syringe; the solution was shaken and rapidly transferred to the cell. A stop-clock was started at the moment of mixing. In the fast runs, the procedure was to set fixed resistances on the box and read the time of balance. In the slow runs, resistances were measured at fixed times. The cells were first filled to overflowing, and the ungreased glass stopper forced in before the first reading was taken. Mercury was placed in the annular cup during the course of the run. To avoid heterogeneity, concentrations were not allowed to exceed 4 mmoles/l.

(4) All runs were followed to completion, *i.e.*, until the resistance was constant, and the contents of the cell were analysed. Owing to the escape of vapour on dissolution of the organic liquid, the superfluous solution left in the mixing flask contained considerably less solute than that in the cell. The concentrations of hydrogen ion and chloride ion, determined by the methods used with methyl chloride, proved to be equal. The specific conductivity κ of the completely hydrolysed solutions led to equivalent conductivities, Λ, which agreed, within the accuracy of the analysis, with the standard values,[6] as the following data at 25° show:

c (mmoles/l.)	3·04	3·81	8·75
$10^{3}\kappa$ (ohm^{-1} $cm.^{-1}$)	1·268	1·581	3·591
Λ ($cm.^{2}$ ohm^{-1} $mole^{-1}$)	417	415	411
Λ (McInnes)	418·0	416·7	412·6

The concentrations of hydrogen chloride in some of the later runs, particularly those followed in dilute solutions, were consequently obtained from the measured values of κ found after the cell had been transferred into a thermostat bath at 25°:

$$c = 10^{6}\kappa_{\infty}/\Lambda \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(5) The products of reaction were also analysed for olefins, by the method of Lucas and Eberz [7] and a slight modification of it, which dispensed with the evacuation and used glass-stoppered titration vessels with a controlled volume of air. The results were negative, but, because of the errors in the analytical method and the small concentrations involved, cannot be taken as conclusive evidence of the complete absence of an elimination reaction. Control experiments with saturated aqueous solutions of 2-methylbut-3-ene gave satisfactory results. Moreover, the product of solvolysis of t-butyl chloride at a concentration of 430 ± 2 mmoles/l. in equimolar methanol–water contained 25·8 mmoles/l. of olefin, indicating an elimination reaction of 6% of the total. A repetition with an initial concentration of 381 gave 27·1 mmoles/l. of olefin. In the mixed solvent, therefore, the percentage elimination is 6·6 ± 0·6%. If the same proportion were formed in pure water, the concentration of olefin would be about 0·26 mmole/l., which is beyond the analytical accuracy. Circumstantial evidence that the presence of olefin in pure water is improbable is provided by Lucas and Eberz,[7] who have shown that isobutene reacts to completion with water to give t-butyl alcohol in acid solution. On the whole, it seems highly probable that the reaction in water is simply $Bu^{t}Cl + H_{2}O \longrightarrow Bu^{t}OH + HCl$.

Results

Examples of results by the fast and the slow technique described above are given in Tables 1 and 2. They are both necessary to illustrate two characteristic features of the experiments, which are a gradual decline of from 1 to 4% in the apparent first-order constant

$$k_{1}' = \frac{1}{t}\ln\frac{\kappa_{\infty} - \kappa}{\kappa_{\infty}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

[6] McInnes, "The Principles of Electrochemistry," Reinhold Publ. Inc., New York, 1939.
[7] Lucas and Eberz, *J. Amer. Chem. Soc.*, 1934, **56**, 460.

when the complete reaction has been followed, and the appearance of a false value of κ_0 when linear extrapolation of ln $(\kappa_\infty - \kappa)$ ignores the data obtained in the early stages of reaction.

The times listed in the first column of each Table are those from the moment when the stop-clock was started, which is as near as is possible to the instant of dissolution. A plot of $\log_{10}(\kappa_\infty - \kappa)$ derived from Table 1 against t (sec.), is strictly linear with a gradient of $-1{\cdot}2605 \times 10^{-3}$, indicating a constant value of $k_1' = 2{\cdot}904 \times 10^{-3}$ sec.$^{-1}$, in agreement with the separate values given in the Table. Equation 2 is seen to be obeyed from the time of the first reading, which corresponds to 67% reaction, to that corresponding to 99·1% reaction. The values in parentheses, which correspond to 99·5 and 99·9% change are ignored. The extrapolated value of $\log_{10}(\kappa_\infty - \kappa)$ is found to be $\bar{4}{\cdot}886$, which is seen to be greater than the true value by 0·021. The difference can be accounted for if a zero-time error of 1·66 sec. is

TABLE 1.

Temp. = 298·20° K. [HCl] = 1·758 mmoles/l. $C = 3{\cdot}452$ cm.$^{-1}$.

Time (sec.)	R (ohms)	$10^4\kappa$ (ohm^{-1} cm.$^{-1}$)	$10^3k_1'$ (sec.$^{-1}$)	Time (sec.)	R (ohms)	$10^4\kappa$ (ohm^{-1} cm.$^{-1}$)	$10^3k_1'$ (sec.$^{-1}$)
0	—	—	—	152	4770	7·238	2·91
40	7000	4·931	2·91	165	4751	7·266	2·89
65	5600	6·165	2·90	190	4731	7·297	(2·85)
78	5300	6·513	2·87	240	4714	7·323	(2·86)
90	5100	6·769	2·89	300	4710	7·330	—
100	5000	6·904	2·89	600	4709	7·331	—
126	4840	7·134	2·91	900	4709	7·331	—

allowed. With most of the fast runs, zero-time errors fell in the range ± 2 sec., and were as often positive as negative.

The data of Table 2, on being similarly analysed, yield, not a constant, but a slowly changing, gradient. For simplicity, we shall analyse the results in two sections, (i) that between $t = 0$ and $t = 390$ sec., when c varies from 0 to 0·66 mmole/l., and (ii) that between $t = 390$ and $t = 5400$ sec., when c changes from 0·66 to 2·49 mmoles/l. In the first section the gradient affords a value of $k_1' = 7{\cdot}41 \times 10^{-4}$ sec.$^{-1}$, and an experimentally permissible zero-time error of 1·05 sec. In the second section, the gradient gives $k_1' = 7{\cdot}03 \times 10^{-4}$ sec.$^{-1}$, and an inadmissibly large zero-time error of 49·4 secs. There is thus a decrease of about 4·5% in k_1' as the reaction proceeds.

TABLE 2.

Temp. = 273·22° K. $[HCl]_\infty = 2{\cdot}55$ mmoles/l. $C = 3{\cdot}452$ cm.$^{-1}$.

Time (sec.)	R (ohms)	$10^4\kappa$ (ohm^{-1} cm.$^{-1}$)	$k_1' \times 10$ (sec.$^{-1}$)	Time (sec.)	R (ohms)	$10^4\kappa$ (ohm^{-1} cm.$^{-1}$)	$k_1' \times 10$ (sec.$^{-1}$)
0	(822,800)	(0·041)	—	1210	8600	4·015	7·06
60	100,000	0·3452	7·37	1432	7800	4·426	7·03
195	36,000	0·9592	7·36	1580	7400	4·666	7·03
275	26,100	1·323	7·48	1765	7000	4·931	7·03
390	19,600	1·761	7·43	1932	6700	5·152	7·03
0	(147,500)	(0·234)	—	2075	6500	5·311	7·05
600	13,900	2·484	6·94	2400	6137	5·624	7·05
656	13,000	2·656	6·96	2700	5892	5·860	7·06
870	10,600	3·257	7·03	3000	5710	6·046	7·06
918	10,280	3·359	6·98	3600	5460	6·323	7·09
986	9800	3·523	6·99	4000	5353	6·449	7·06
1016	9600	3·596	7·00	5400	5159	6·691	7·01
1068	9300	3·712	7·00	∞	5047	6·841	—
1125	9000	3·858	7·07				

If the equivalent conductance, Λ, of hydrogen chloride in water were independent of its concentration, c, it could be concluded that the rate of chemical change also decreases as the reaction proceeds. Such, of course, is not the case, and the unimolecular constant, k_1, governing the chemical change is related to the apparent constant k_1' as follows:

$$k_1 = -\frac{\mathrm{d}\ln(c_\infty - c)}{\mathrm{d}t} = -\frac{\mathrm{d}\ln(\kappa_\infty - \kappa)}{\mathrm{d}t} \cdot \frac{\mathrm{d}\ln(c_\infty - c)}{\mathrm{d}\ln(\kappa_\infty - \kappa)} = k_1' f \quad . \quad . \quad (3)$$

To evaluate the function f, it will suffice to assume the validity of the limiting conductance

law $\Lambda = \Lambda_0 - Ac^{\frac{1}{2}}$, although in fact a more elaborate equation is required to cover the complete run. Then

$$f = \left[1 - \frac{A}{\Lambda_0}\left(\frac{c_\infty^{\frac{3}{2}} - c^{\frac{3}{2}}}{c_\infty - c}\right)\right]\left[1 - \frac{3}{2}\frac{A}{\Lambda_0} \cdot c^{\frac{1}{2}}\right]^{-1} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

For hydrogen chloride in water at 25°, $A/\Lambda_0 = 0{\cdot}0113$. Thus in a solution for which $c_\infty = 2{\cdot}5$ mmoles/l., f increases from an initial value of 0·982 to a final value of 1·028, *i.e.*, by 4·7%. For the same electrolyte at 0°, a theoretical estimate of A/Λ_0 based on Onsager's equation is 0·01056. At this temperature, f for a solution of the same concentration increases from 0·983 at $c = 0$ to 1·026 at $c = 2{\cdot}5$, *i.e.*, by 4·3%. That these corrections from conductivity data should lie so very close to the kinetic deviations may be to some extent fortuitous, because no allowance has been made for the presence of t-butyl alcohol. This effect, however, has been shown to be very small, and the magnitude and direction of change of the function f are consequently taken as firm evidence that the unimolecular velocity coefficient k_1 governing the hydrolysis of t-butyl chloride in water is in fact a true constant.

Effect of Added Electrolytes.—The results summarised in Table 3 show that there is a slight positive electrolyte effect, the gradient of $\log_{10} k_1/dc$ being approximately 520 ± 20. Two theories which strive at a quantitative formulation of the salt effect in reactions of this type have been critically compared and found to be almost equally adequate.[8] The Table also shows that alkali at concentrations exceeding that of the reactant has no effect on the rate of hydrolysis. The result is similar to that first found by E. D. Hughes [2] for the first-order constant governing the solvolysis of t-butyl chloride in mixed solvents.

Effect of Temperature.—The temperature effect cannot be summarised in the form of the integrated equation of Arrhenius, $k_1 = A \exp(-E_A/\boldsymbol{R}T)$, but is adequately reproduced (Table 4) by the equation:

$$\log_{10} k_1 \text{ (in sec.}^{-1}) = 280{\cdot}870 - 91{\cdot}586 \log_{10} T - 16631{\cdot}75/T \quad . \quad . \quad . \quad (5)$$

It follows that the apparent energy of activation, defined as $-\boldsymbol{R}[\mathrm{d} \ln k_1/\mathrm{d}(1/T)]$, is

$$E_A \text{ (cal./mole)} = 76{,}102 - 182T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

In this respect the hydrolysis of t-butyl chloride resembles that of methyl chloride and the other methyl halides. According to equation (5), k_1 at 0° and 25° are $6{\cdot}94 \times 10^{-4}$ and $2{\cdot}91 \times 10^{-3}$ sec.$^{-1}$ respectively, which differ by only a few per cent from the values of $7{\cdot}27 \times 10^{-4}$ and $2{\cdot}70 \times 10^{-3}$ found by Winstein and Fainberg.[4] At the mid-point of this temperature range, their data give $E_A = 23{,}400$ cal. mole^{-1}, which again differs little from the value of 24,112 given by equation 6. If, however, we accept the empirical equation used by them, their E_A value would appear to be 23,790, which is in closer agreement with the present value. Their data at the two temperatures used are thus, on the whole, fully corroborated.

TABLE 3. *The effect of dilution and of added electrolytes at* 292·90° K.

[Bu^{t}Cl]	Electrolyte	[Electrolyte] (mmole/l.)	Mean $k_1 \times 10^3$	Standard error
0·64	None		1·4460	0·0114
1·06	,,		1·4675	0·0036
3·91	,,		1·4637	0·0082
4·08	,,		1·4959	0·0072
4·36	HCl	8·75	1·5173	0·0060
4·46	NaOH	13·5	1·4817	0·0037
2·04	KCl	100·0	1·6749	0·0135

TABLE 4. *Observed and calculated unimolecular constants for the hydrolysis of t-butyl chloride in water.*

Temp. (°K)	273·22°	281·33°	287·01°	292·90°	298·20°
$10^4 k_1$ (sec.$^{-1}$): obs.	7·02	27·3	64·9	148	292
eqn. (5)	6·984	27·38	64·97	147·8	292·1

[8] Nash and Monk, *J.*, 1955, 1899.

The values of k_1 and E_A found by Heppolette and Robertson [2] for the hydrolysis of methyl chloride lie approximately midway between the two values published by the present author. As their method is probably more accurate than his, their results are here accepted. They lead to the comparison summarised in Table 5. t-Butyl chloride is seen to be hydrolysed faster

TABLE 5. *Comparison of the rates and energies of activation for the hydrolysis of methyl and t-butyl chloride.*

Solute	k_1 at 298·16° K (sec.$^{-1}$)		E_A at 298·16° K (cal./mole)	
MeCl	$2{\cdot}35 \times 10^{-8}$	Ratio = $1{\cdot}24 \times 10^6$	26,562	Difference = 4725
Bu^{t}Cl	$2{\cdot}91 \times 10^{-2}$		21,837	

than methyl chloride by a factor of at least 10^6. To attribute the observed ratio entirely to a difference in activation energies would require the difference to be 8312 cal./mole. Thus the change in k_1 is due in roughly equal measure to a change in E_A and to a change in those terms which correspond to the first constant A of the integrated equation of Arrhenius.

DISCUSSION

(1) *Hydrolysis.*—The unimolecular constants, k_1, of uncatalysed reactions which have been accurately examined in aqueous solutions can usually be represented by equations of the form:

$$\log_{10} k_1 = a_1 - b_1 \log_{10} T - c_1/T$$

They include the hydrolysis of methyl fluoride,[9] the remaining methyl halides,[2] methyl nitrate,[10] and methylene dichloride,[11] and the following reactions not generally regarded as hydrolyses: the mutarotation of α-xylose, α-mannose, α-glucose, and α-lactose;[12] the decarboxylation of trichloroacetic acid, tribromoacetic acid, and trinitrobenzoic acid;[13] and the decomposition of benzenediazonium chloride.[14] The average value of b_1 for the hydrolyses is 26·6, indicating that the heat capacity of the activated complex is less by about 53 cal. mole^{-1} degree^{-1} than that of the reactants in their normal state. In the equation independently adopted by Pitzer [15] and the writer [16] to express the temperature variation of the ionisation constant of numerous weak electrolytes in water,

$$\log_{10} K = A - B \log_{10} T - C/T$$

the term B has an average value of about 20·6, indicating that the sum of the C_P terms for the products of ionisation is less than that for the un-ionised molecule by about 41 cal. mole^{-1} degree^{-1}. Both b_1 and B have been interpreted in terms of the freezing-in of certain degrees of freedom of the water molecules.[17] Since ΔC_P for the fusion of ice at 25° C is about 8·1 cal. mole^{-1} degree^{-1}, the activation of solutes during hydrolysis and the ionisation of weak electrolytes could be ascribed to the freezing-in of between 5 and 7 molecules of liquid water. There are, of course, many other factors to be reckoned with and different explanations discussed in the papers cited [2,3] are possible. This crude method suffices to emphasise the analogy between the unimolecular hydrolysis of solutes in water and the process of ordinary ionisation. The principal difference between them

[9] Glew and Moelwyn-Hughes, *Proc. Roy. Soc.*, 1952, *A*, **211**, 254.
[10] McKinley-McKee and Moelwyn-Hughes, *Trans. Faraday Soc.*, 1952, **48**, 247.
[11] Fells and Moelwyn-Hughes, *J.*, 1958, 1326.
[12] Kendrew and Moelwyn-Hughes, *Proc. Roy. Soc.*, 1940, *A*, **176**, 352.
[13] Johnson and Moelwyn-Hughes, *Proc. Roy. Soc.*, 1940, *A*, **175**, 118.
[14] Moelwyn-Hughes and Johnson, *Trans. Faraday Soc.*, 1940, **36**, 948.
[15] Pitzer, *J. Amer. Chem. Soc.*, 1937, **59**, 2365.
[16] Moelwyn-Hughes, *Trans. Faraday Soc.*, 1938, **34**, 91.
[17] Ulich, *Z. Elektrochem.*, 1930, **36**, 497.

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is that only the anion formed in the primary process is present in solution at the end of a hydrolytic change, whereas both anion and cation are present after the establishment of an ionisation equilibrium. Since the hydrolyses hitherto examined show no trace of consecutive reactions, it is to be inferred that the cation initially formed in hydrolytic reactions reacts rapidly with water. This conclusion,[2] it will be appreciated, is precisely that drawn from evidence of quite a different nature by Hughes and Ingold.[3] An upper limit to the half-life of the t-butyl ion can be estimated from the results given here, since the method is sensitive enough to have detected a consecutive change if it were 100 times faster than the first change. At 25° c, therefore, the half-life of the ion cannot exceed 0·2 sec.

(2) *Substitution.*—In aqueous solutions of methyl and ethyl halides containing reactive ions [18] such as $S_2O_3^{2-}$ or OH^-, the unimolecular hydrolysis $RX + H_2O \longrightarrow ROH + H^+ + X^-$ is accompanied by the bimolecular substitution $RX + Y^- \longrightarrow RY + X^-$. In aqueous solutions containing moderate concentrations of hydroxyl ions, however, the substitution reaction $Bu^tCl + OH^- \longrightarrow Bu^tOH + Cl^-$ does not occur. This result fully confirms for the reaction in water the effect first noted by E. D. Hughes [3] for the same solute in ethanol–water and in acetone–water mixtures. The energy of activation of such substitutions has not yet been satisfactorily evaluated, but it is thought to consist of a number of components, among which is the energy required to overcome the intrinsic repulsion between the ion and the molecule when they are in the close contact necessary for reaction. It is natural to expect this energy to be much greater for the pair OH^-, Bu^tCl than for the pair OH^-, MeCl, and the velocity of substitution reaction may become so small as to be negligible. This is the plausible interpretation of the steric effect given by Hughes and Ingold.[3] In the present example, even if the velocity of the reaction $Bu^tCl + OH^- \longrightarrow Bu^tOH + Cl^-$ were to be no slower than that of the reaction $MeCl + OH^- \longrightarrow MeOH + Cl^-$, it would still be many hundreds of times too slow to affect the net rate of reaction by a few per cent.

Another explanation of the effect may be given in terms of the idea of partial desolvation. If one water molecule of the four that are attached to the hydroxyl ion has to be removed before the ion can effect substitution, a lower limit to the energy of activation is automatically set, irrespective of the facility with which the carbon–halogen bond is broken.

The author is indebted to Mr. G. G. Yates of the Cavendish Laboratory for designing the circuit.

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[18] Moelwyn-Hughes, *J.*, 1933, 1576; Nielsen, *J. Amer. Chem. Soc.*, 1936, **58**, 206; Moelwyn-Hughes, *J.*, 1938, 779; *Proc. Roy. Soc.*, 1949, *A*, **196**, 540.

298. *The Kinetics of the Reaction between Methyl Fluoride and Lithium Iodide in Acetone Solution.*

By FARHAT-AZIZ and E. A. MOELWYN-HUGHES.

The reaction between methyl fluoride and lithium iodide has been investigated in acetone solution in the absence of the vapour phase. The reversible reactions $MeCl + I^- \rightleftharpoons MeI + Cl^-$ have been studied in the same solvent, by using lithium and potassium iodide. Complications arise owing to the low degree of ionisation of lithium chloride and the low solubility of potassium chloride. As far as quantitative allowance can be made for these effects, there appears to be no appreciable cationic effect on the velocity of reaction. A comparison of the rates of reaction of the iodide ion with methyl fluoride, chloride, and bromide shows that the entire effect of substitution is to alter the energy of activation E_A in the equation $k_2 = A \exp(-E_A/\boldsymbol{R}T)$. A has the normal value of about 2×10^{11} l. mole^{-1} sec.$^{-1}$. E_A changes by 7000 cal., and the rates of reaction at 25°c by a factor of about 77,000.

THE object of this work was to obtain further experimental information on reactions of the type $MeX + Y^- \longrightarrow MeY + X^-$ in acetone solution, and in particular to examine a reaction where X is F.

EXPERIMENTAL

Materials.—Acetone, methyl chloride, and lithium iodide were of the purity described earlier.[1] Potassium iodide was recrystallised from distilled water and dried at 120° for several hours. Methyl fluoride was prepared by Lawson and Collie's method.[2] A 25% solution of tetramethylammonium hydroxide was neutralised with hydrogen fluoride, and the solution was evaporated at a low heat to the point of crystallisation. After cooling, the crystals were separated. It was not found possible to separate the crystals completely from the mother-liquor; they were dried in a vacuum at 160° for several hours. The dried salt was then decomposed into trimethylamine and methyl fluoride by raising the temperature to 180—210°. The issuing gases were passed through a trap cooled by solid carbon dioxide and acetone, and condensed in a receiver cooled by liquid air. The collected sample was passed through four evacuated bubblers containing concentrated sulphuric acid except that the second contained 33% potassium hydroxide solution, then over soda-lime, anhydrous calcium chloride, and phosphoric oxide, and was finally collected in a receiver cooled in liquid air. The purification was repeated and the material thrice fractionally distilled, the middle portion being retained in each operation. The final sample of methyl fluoride was pure by gas-chromatographic and spectrographic standards. The vapour pressures measured at three temperatures are shown in Table 1, along with the vapour pressure given by other investigators. Temperatures were measured with a platinum resistance thermometer calibrated by the National Physical Laboratory.

TABLE 1. *The vapour pressure of methyl fluoride.*

	Vapour pressure (mm. of mercury)		
Temperature	Moles and Batuecas [3]	Michels and Wassenaar [4]	This work
−82·053°	608·0	615·1	610·9
−78·321	750·8	759·4	755·2
−78·274	752·6	761·3	756·8

Solutions of the methyl halides and the alkali-metal salts in acetone were prepared as previously described.[1]

Reaction between Methyl Fluoride and Lithium Iodide in Acetone.—This reaction was studied in the absence of a vapour phase in a reaction previously described.[1] Solutions of methyl

[1] Farhat-Aziz and Moelwyn-Hughes, *J.*, 1959, 2635.
[2] Lawson and Collie, *J.*, 1888, **53**, 624.
[3] Moles and Batuecas, *J. Chim. phys.*, 1919, **17**, 537.
[4] Michels and Wassenaar, *Physica*, 1948, **14**, 104.

fluoride in acetone (~70 mmoles/l.) and of lithium iodide of known strengths were brought to the working temperature, mixed, and poured into the reaction vessel. The reaction was followed by removing samples through a cotton-wool filter at measured time intervals, chilling to 0°, pipetting 5 c.c. into 10 c.c. of distilled water, adding 5 c.c. of 50% w/v sulphuric acid and 15 c.c. of acetone, and then titrating the mixture for inorganic iodide against standard ceric sulphate solution with ferroin as indicator.[5] The initial concentration of inorganic iodide was estimated by the same method at zero time.

The initial reaction mixture and the products were also analysed by gas-chromatography. The column contained 16% polyethylene glycol (*M* 400) on 60—80 mesh Silocel C.22. The column was 8 feet long. Hydrogen was used as carrier gas. The analysis showed that reaction goes to completion (Figs. 1 and 2). The distinctive peak of methyl fluoride in Fig. 1 has completely disappeared in Fig. 2. The peak for oxygen in both figures is attributable to oxygen absorbed in the acetone. The peaks of diethyl ether are internal standards.

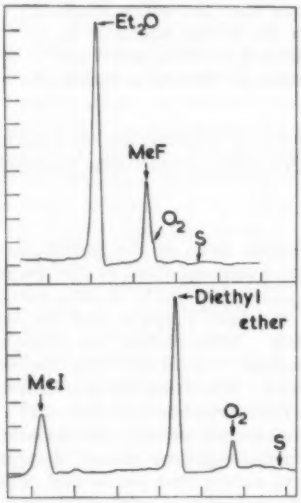

FIG. 1.

Gas-chromatograms of (FIG. 1) *methyl fluoride in ether and* (FIG. 2) *reaction product in ether.*

S = *sample injected.*

FIG. 2.

Runs carried out at 50° were followed to completion and the difference between the initial and the final concentrations of inorganic iodide gave the initial concentration of methyl fluoride. Runs at lower temperatures were too slow to be carried to their ends. In these cases, a sample of the mixture was sealed in a glass tube previously filled with nitrogen and heated for about two weeks at 50° to complete the reaction. The inorganic iodide was estimated and the initial concentration of methyl fluoride was then calculated. Incubation of the reaction mixture at 100° proved to be analytically unsuitable.

The reaction mixture stays clear to the naked eye, though lithium fluoride crystallises during the initial stages of the reaction. Temperatures were kept constant to within ±0·03°. The medical absorbent cotton wool used for filtration was washed with boiling distilled water and with acetone before being dried in an oven at low temperatures.

Kinetic Results.—As the reaction appears to be free from complications the usual second-order equation

$$k_2 = \frac{1}{t(b-a)} \ln \frac{a(b-x)}{b(a-x)}$$

can be used, where a and b are the initial concentrations of methyl halide and inorganic iodide, and x is the concentration of soluble product at time t. On the assumption that the rate-measuring step in the reaction between methyl fluoride and the iodide ion is $MeF + I^- \longrightarrow MeI + F^-$, we must modify this equation to allow for incomplete ionisation of lithium iodide, by replacing $(b-a)$ with $(b-a)\alpha_\infty$, b with $b\alpha_0$, and $(b-x)$ with $(b-x)\alpha$, where α_0, α_∞, and α

[5] Lewis, *Ind. Eng. Chem. Analyt.*, 1936, **8**, 199.

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are the degrees of ionisation of lithium iodide in acetone initially, finally, and at time t respectively. The modified equation is:

$$k_2 = \frac{1}{t(b-a)\alpha_\infty} \ln \frac{a(b-x)\alpha}{b(a-x)\alpha_0} \quad \ldots \ldots \ldots \quad (1)$$

This equation is not rigorous.

Degrees of ionisation of lithium iodide in acetone solution have been derived from Blokker's data.[6] The results of a typical run are given in Table 2. The most reliable values of the second-order velocity constant k_2 are those calculated for points corresponding to 1/4, 1/2, and 3/4 of the complete reaction.

TABLE 2. *Bimolecular velocity constant k_2 for the reaction* $MeF + I^- \longrightarrow MeI + F^-$ *in acetone.*

Temp. = 50·00°; $[MeF]_0$ = 33·4 mmoles/l.

Time (hr.)	$[LiI]_t + [I^-]_t$ (mmoles/l.)	α	$10^4k_2 \times 10^4$ (l. mole^{-1} sec.$^{-1}$)	Time (hr.)	$[LiI]_t + [I^-]_t$ (mmoles/l.)	α	$10^4k_2 \times 10^4$ (l. mole^{-1} sec.$^{-1}$)
0·00	212·4	0·162	—	143·00	180·4	0·173	1·93
1·008	211·4	0·162	2·28	∞	179·0	0·173	—
3·004	209·6	0·163	2·41				Mean = 2·04
10·007	206·0	0·164	1·74	$t_{\frac{1}{2}}$ = 10·50	204·1	0·164	2·22
22·00	197·4	0·167	2·26	$t_{\frac{1}{4}}$ = 26·75	195·7	0·167	2·15
46·50	190·7	0·169	1·90	$t_{\frac{1}{2}}$ = 66·40	187·4	0·170	1·77
79·50	185·4	0·171	1·77				Mean = 2·05

Accepted value of $k_2 = 2·05 \times 10^{-4}$ l./mole^{-1} sec.$^{-1}$.

The values of k_2 similarly obtained at different temperatures are summarised in Table 3. A systematic study of the effect of a change in the concentration of either reactant was not attempted. The Arrhenius equation obtained by the method of least squares is:

$$k_2 = 2·01 \times 10^{11} \exp(-22{,}190/\boldsymbol{R}T)$$

Values of k_2 reproduced by this equation are given in the fifth column of Table 3.

TABLE 3. *Bimolecular velocity constant k_2 in l. mole^{-1} sec.$^{-1}$ for the reaction* $MeF + I^- \longrightarrow MeI + F^-$ *in acetone.*

Temperature	$[MeF]_0$ (mmole/l.)	$[LiI]_0 + [I^-]_0$ (mmole/l.)	10^4k_2 Obs.	Calc.
25·00°	51·2	211·9	0·110	0·108
40·06	40·9	209·9	0·631	0·660
50·00	33·4	212·4	2·05	1·99

Cationic Effect in the Reaction between Methyl Chloride and Iodide Ion in Acetone.—The kinetics of the reaction between these materials in acetone have been studied before with lithium iodide as a source of I^-. To explore any possible specific effect due to a change in the cation, the same reaction has been investigated with potassium iodide as a source of I^-. The experimental conditions, unfortunately, are not quite comparable, because potassium chloride is only slightly soluble in acetone (1×10^{-5} mole/l.) [7] and the reaction from its initial stages becomes heterogeneous.

Procedure.—Kinetic and static aspects of the reaction between methyl chloride and potassium iodide in acetone have been studied by using an earlier type of vessel where mercury is used to exclude the vapour phase.[8] A vessel of the latest type [1] was used for a few equilibrium runs. Solutions of the reactants in acetone were separately prepared for each run, and samples were expressed through cotton-wool plugs as used in the methyl fluoride–lithium iodide reaction. Chilled samples were analysed for inorganic iodide by two methods. First, 5 c.c. of 50% w/v sulphuric acid and 5 c.c. of acetone were added, and the whole mixture was titrated against ceric sulphate solution for inorganic iodide with ferroin as indicator. Secondly, 5 c.c. of the same sample were evaporated under a vacuum, the residue was dissolved in 15—20 c.c. of water, and the solution was titrated against silver nitrate for total inorganic halides with dichlorofluorescein as indicator. The two titrations always agreed within the experimental error, showing the precipitation of potassium chloride to be quantitative.

The initial concentration of inorganic iodide was determined by both methods.

[6] Blokker, *Rec. Trav. chim.*, 1935, **54**, 975.
[7] Lannung, *Z. phys. Chem.*, 1932, *A*, **161**, 255.
[8] Moelwyn-Hughes, *Trans. Faraday Soc.*, 1941, **37**, 279.

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To determine the initial concentration of methyl chloride, 5 c.c. of the reaction mixture were sealed with excess of N-sodium hydroxide in a glass tube and heated at 100°, for about 24 hr. to ensure complete hydrolysis. The hydrolysed sample was estimated for total halide by the silver nitrate method (with dichlorofluorescein in the presence of dextrin as a protective colloid). In some of the equilibrium runs, the concentrations of methyl chloride and iodide were estimated at equilibrium positions. The hydrolysed sample was neutralised with 33% acetic acid and then evaporated to dryness at a low heat. The residue was extracted with hot distilled water and washed. The filtrate was made up to 100 c.c. Portions (20 c.c.) were titrated against silver nitrate in the presence of 1 c.c. of N-ammonium carbonate and 4—6 drops of eosin adsorption indicator for iodide. Other parts (20 c.c.) were titrated for total inorganic halide by the silver nitrate method described above. The concentrations of total methyl halides, methyl chloride, and methyl iodide were thus obtained. The concentration of methyl iodide estimated at the equilibrium position was always in very good agreement with the decrease in the initial concentration of inorganic iodide. This fact again shows that potassium chloride is quantitatively precipitated.

Temperatures were kept constant to within $\pm 0{\cdot}03°$. The reaction mixture became turbid during its initial stages but cleared within 0·5 hr., though the precipitation of potassium chloride continued. The time taken to reach transparency increased as the temperature was lowered.

Static Results.—Constancy of the expression, $K = [\mathrm{MeI}][\mathrm{Cl^-}]/[\mathrm{MeCl}][\mathrm{I^-}]$, can reasonably be expected, and, if the solubility product L of potassium chloride is constant, we have $L = [\mathrm{K^+}][\mathrm{Cl^-}]$, which in the present system is effectively $L = [\mathrm{I^-}][\mathrm{Cl^-}]$. Hence $K = [\mathrm{MeI}]L/[\mathrm{MeCl}][\mathrm{I^-}]^2$. It was found, however, that $K'' = K/L$ was variable, but that the expression $K' = [\mathrm{MeI}]/[\mathrm{MeCl}][\mathrm{I^-}]$ was constant. This suggests that the concentration of $\mathrm{Cl^-}$ in contact with crystalline potassium chloride under our experimental conditions remains constant throughout the reaction. The values of $1/K'$ at different temperatures and concentrations of the reactants have been summarised in Table 4. The iodide-ion concentration was obtained by using the degree of ionisation of potassium iodide in acetone derived from the data of Walden,[9] Fischler,[10] Walden, Ulich, and Busch,[11] Lannung,[7] Blokker,[6] and Dippy and Hughes.[12] A critical survey is given elsewhere.[13] For comparison, the value of $1/K''$ are also summarised in Table 4. The experimental values of K' are reproduced by the equation

$$\ln K' = (31{\cdot}03/\boldsymbol{R}) - (5565/\boldsymbol{RT})$$

With the concentrations shown in Table 4 it takes 5—6 weeks to reach equilibrium at 20°.

TABLE 4. *Equilibrium constants for the reaction* $\mathrm{MeCl} + \mathrm{I^-} \rightleftharpoons \mathrm{MeI} + \mathrm{Cl^-}$ *in acetone solution:* $K' = [\mathrm{MeI}]_\infty/[\mathrm{MeCl}]_\infty[\mathrm{I^-}]_\infty$, $K'' = [\mathrm{MeI}]_\infty/[\mathrm{MeCl}]_\infty[\mathrm{I^-}]_\infty^2$.

Temp.	$[\mathrm{MeCl}]_0$	$[\mathrm{KI}]_0 + [\mathrm{I^-}]_0$ (mmoles/l.)	$[\mathrm{KI}]_\infty + [\mathrm{I^-}]_\infty$	α_∞	$10^6/K''$ (moles/l.²)	$10^3/K'$ (moles/l.²) obs.
20·00°	35·55	29·65	6·56	0·659	10·1	2·33
20·00	53·16	15·33	$1{\cdot}00_6$	0·850	1·98	2·32
					Accepted =	2·33
25·00	—	—	—	—	—	(2·00)
30·00	18·02	30·35	15·61	0·513	14·3	1·78
30·00	52·91	30·33	$1{\cdot}66_2$	0·790	1·46	1·11
30·00	35·55	29·65	5·59	0·657	6·44	1·75
30·00	53·16	15·33	$0{\cdot}946_4$	0·850	1·74	2·17
					Mean =	1·70
40·00	18·02	30·35	15·25	0·496	11·1	1·46
40·00	52·91	30·33	$1{\cdot}49_3$	0·702	1·17	0·987
40·00	35·55	29·65	4·56	0·664	3·82	1·26
					Mean =	1·24
50·00	52·91	30·33	$1{\cdot}46_2$	0·783	1·09	0·954
50·00	34·81	29·14	3·84	0·668	2·47	0·964
50·00	53·16	15·33	0·404	0·920	0·354	0·952
					Mean =	0·957

[9] Walden, *Z. phys. Chem.*, 1907, **59**, 196, 207.
[10] Fischler, *Z. Elektrochem.*, 1913, **19**, 131.
[11] Walden, Ulich, and Busch, *Z. phys. Chem.*, 1926, **123**, 429.
[12] Dippy and Hughes, *J.*, 1954, 953.
[13] Farhat-Aziz, Thesis, Cambridge, 1959.

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Kinetic Results.—If the reactions occur exclusively between the polar molecules and the halide ions we have:

$$MeCl + I^- \underset{k_4}{\overset{k_2}{\rightleftharpoons}} MeI + Cl^-$$

With the earlier notation and the constant concentration of Cl^- denoted by s, the rate equation becomes:

$$dx/dt = k_2(a - x)(b - x)\alpha - k_4 xs \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

This equation cannot be integrated because α is a function of $(b - x)$, but if α is regarded as constant during a run and given the mean of its initial and final values then the equation can be integrated to give: [11]

$$k_2\alpha = \frac{1}{2\beta bt} \ln\left[\frac{a - (\gamma - \beta)x}{a - (\gamma + \beta)x}\right] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where

$$\gamma = \tfrac{1}{2}\left[1 + \frac{a}{b} + \frac{1}{K'b\alpha}\right] \text{ and } \beta^2 = \gamma^2 - \frac{a}{b}$$

The α of ref. 14 is γ in our case.

Only the velocity constant k_2 for the direct reaction $MeCl + I^- \longrightarrow MeI + Cl^-$ can be found, because s is not known. Values of k_2 have been calculated by two methods. First, equation (2) has been used in its incremental form, by drawing tangents to the progress curve. Secondly, equation (3) has been used directly. The first method is physically superior because it involves no assumption concerning α. The values of k_2 obtained from it are the accepted values. Some of the kinetic runs were not followed to completion. Values of k_2 obtained by both methods for a specimen run are compared in Table 5. They sometimes show a falling trend with the progress of reaction but this is not general.

TABLE 5. *Bimolecular velocity constant k_2 for the reaction* $MeCl + I^- \longrightarrow MeI + Cl^-$ *in acetone.*

Temp. = 30·00°. $[MeCl]_0$ = 24·15 mmoles/l.

Time (min.)	$[KI]_t + [I^-]_t$ (mmoles/l.)	α	10^4k_2 (l. mole^{-1} sec.$^{-1}$) by eqn. (3)	by eqn. (2)
0	42·28	0·408	—	—
—	38·99	0·418	—	16·8
—	37·01	0·421	—	18·8
150	36·39	—	17·9	—
—	33·19	0·431	—	17·4
—	30·98	0·438	—	18·2
—	29·41	0·441	—	16·7
570	28·47	—	17·6	—
1230	25·39	—	13·2	—
1890	22·97	—	15·5	—
3061	21·99	—	15·7	—
—	18·13	0·493	—	—
				Mean = 17·6

Values of k_2 obtained by the incremental method for runs with different initial concentrations at different temperatures are summarised in Table 6. They show that k_2 is not sensibly affected by changes in the initial concentrations. The calculated values are those reproduced by the Arrhenius equation:

$$k_2 = 6{\cdot}98 \times 10^{11} \exp(-20{,}250/\boldsymbol{RT})$$

Comparison of the Velocity Constants k_2 for the reaction $MeCl + I^- \longrightarrow MeI + Cl^-$ *obtained with Lithium and Potassium Salts.*—A comparison of the experimental values of k_2 in the two systems (Table 7) shows that the reaction is somewhat faster with lithium than with potassium iodide. The apparent difference in the values of k_2 decreases with a rise in temperature and their ratio approximates to unity at the highest temperature examined. The absolute values

[14] Moelwyn-Hughes, *Trans. Faraday Soc.*, 1949, **45**, 167.

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of k_2 depend to some extent on the degrees of ionisation adopted. These, in turn, have been derived from the conductivity data of many investigators.

TABLE 6. *Accepted bimolecular velocity constant k_2 for the reaction* $MeCl + I^- \longrightarrow MeI + Cl^-$ *in acetone.*

Temp.	$[MeCl]_0$	$[KI]_0 + [I^-]_0$ (mmoles/l.)	10^4k_2 (l. mole^{-1} sec.$^{-1}$) obs.	calc.
20·00°	15·97	30·56	5·56	5·54
25·00	—	—	—	9·86
30·00	28·14	42·95	16·8	—
30·00	24·15	42·28	17·6	—
30·00	16·06	30·52	17·3	—
30·00	35·85	30·48	16·9	—
30·00	15·74	30·36	18·0	—
			Mean = 17·3	17·5
40·00	17·61	31·66	50·6	—
40·00	16·00	30·18	50·1	—
			Mean = 50·4	50·6
50·00	15·43	29·86	147	—
50·00	35·56	29·67	136	—
			Mean = 142	139

TABLE 7. 10^4k_2 (l. mole^{-1} sec.$^{-1}$) *for the reactions* $MeCl + I^- \longrightarrow MeI + Cl^-$ *in acetone.*

Temp.	With LiI	With KI	Ratio
20°	8·08	5·56	1·45
30	24·8	17·3	1·43
40	65·2	50·4	1·30
50	157	142	1·11

The uncertainty thus introduced makes it impossible to distinguish between the two sets of constants. The experimental evidence is clearly insufficient to establish any real specific effect of the cation on the rate of reaction. With either salt at 50°, $k_2 = 1{\cdot}5 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$, with a possible error of 5%. E_A for the reaction with LiI is 18,610 cal./mole, and with KI is 20,250. If we accept the mean value of $E_A = 19{,}430 \pm 820$, we obtain the equation

$$k_2 = 2{\cdot}07 \times 10^{11} \exp(-19{,}430/\boldsymbol{R}T)$$

DISCUSSION

Comparison of the Kinetics of the Reactions of the Iodide Ion with Three Methyl Halides in Acetone Solution.—Table 8 summarises what it known on the kinetics of the reactions between the iodide ion and methyl halides in acetone solution.

TABLE 8.

Reaction	10^5k_2 at 298·16°K (l. mole^{-1} sec.$^{-1}$)	$10^{-11}A$ (l. mole^{-1} sec.$^{-1}$)	E_A (cal./mole)
$MeF + I^- \longrightarrow MeI + F^-$	1·08	2·01	22,190
$MeCl + I^- \longrightarrow MeI + Cl^-$ ...	119	2·07	19,430 ± 820
$MeBr + I^- \longrightarrow MeI + Br^-$ ...	82,700	1·04	15,140 ± 1200

The last entry is based on earlier data [14] which have been corrected for the ionisation of potassium iodide at the various concentrations and temperatures employed. Unlike the other entries, the last one refers to systems containing the vapour phase. The same drawback attaches to later work on this reaction (Evans and Hamann; [15] Fowden, Hughes, and Ingold [16]). Despite this uncertainty there seems little doubt that, in this sort of reaction, changes in the velocity constants are due to changes in the activation energy, E_A.

[15] Evans and Hamann, *Trans. Faraday Soc.*, 1951, **47**, 30.
[16] Fowden, Hughes, and Ingold, *J.*, 1955, 3187.

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The term A of the Arrhenius equation $k_2 = A \exp(-E_A/RT)$ is sensibly constant, though the absolute rates of reaction differ by a factor of 77,000. It happens, also, that E_A is a fairly constant fraction of the dissociation energy D_e of the carbon–halogen bond in the gas phase ($E_A/D_e = 0{\cdot}24$), as expected by Ogg and Polanyi.[17] In acetone solution there is thus no evidence that the energy required partially to desolvate the anion contributes significantly to the energy of activation, as it may well do in aqueous solution.[18]

[*Added in proof.*] Since this paper was communicated, Winstein, Savedoff, Smith, Stevens, and Gall (*Tetrahedron Letters*, 1960, No. 9, 24) have published kinetic results on the reaction of n-butyl *p*-bromobenzenesulphonate with lithium chloride, bromide, and iodide and with tetra-n-butylammonium chloride, bromide, and iodide in acetone solution. They confirm our conclusions that the rate-determining step is the bimolecular reaction between the organic molecule and the halogen ion, and that there is no specific effect due to the cation.

One of us is indebted to the Royal Commission for the Exhibition of 1851 for an Overseas Research Scholarship and to the Government of Pakistan and the authorities of the University of Cambridge for financial help.

Department of Physical Chemistry, Cambridge. [*Received, October 5th*, 1960.]

[17] Ogg and Polanyi, *Trans. Faraday Soc.*, 1935, **31**, 615.
[18] Bathgate and Moelwyn-Hughes, *J.*, 1959, 2642.

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299. *Steric Effects in Di- and Tri-arylmethanes. Part V.*[1] *Electronic Absorption Spectra of Derivatives of Malachite Green containing* ortho-*Substituents in the Dimethylaminophenyl Groups.*

By C. C. Barker and G. Hallas.

Spectral changes caused by the crowding effect of substituents in the 2′- and 2′,2″-positions of Malachite Green are described and discussed. The increase in intensity of the *x*-band which was previously reported to occur when substituents are introduced into the 2-position also occurs when substituents are already in the 2′- and 2′,2″-positions.

In Part III [2] of this series it was shown that *ortho*-substituents in the phenyl group of Malachite Green (I) produce unexpected increases in the intensity of the first absorption band (*x*-band) which also shows small bathochromic shifts. At the same time, hypsochromic shifts and reductions in intensity are produced in the second band (*y*-band). These effects are the results of conformational changes brought about by the *ortho*-substituents, but a precise interpretation cannot be put forward at present because of the large number of such changes possible in an unsymmetrical trinuclear dye of this type. The spectra of derivatives of Malachite Green containing *ortho*-substituents in the dimethylaminophenyl groups have therefore been examined.

A 2′-methyl group in Malachite Green produces a bathochromic shift and reduction in intensity of the *x*-band (Table 1), and this effect is consistent with rotation of one or both of the dimethylphenyl groups about the central bond(s), the purely electronic effect of the methyl group being hypsochromic. However, such rotation should result in increased departure from uniplanarity along the unsymmetrical *y*-axis of the molecule and thus lead to a hypsochromic shift and reduction in intensity of the *y*-band, whereas the observed shift is bathochromic and the intensity remains constant (Table 1). The introduction of a second methyl group into the 2″-position exaggerates these spectral changes

[1] Part IV, *J.*, 1961, 1395.
[2] Part III, *J.*, 1961, 1285.

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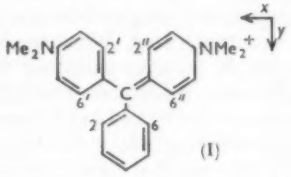
and causes a slight reduction in $\varepsilon_{max.(y)}$ from 20,000 to 18,000. Tentatively, these bathochromic shifts of the *y*-band may be attributed to the greater electronic symmetry along the *y*-axis which results from displacement of charge on to the phenyl group by rotation of the dimethylaminophenyl groups about the central bonds. These spectral shifts are



(I) (II) $(p\text{-Me}_2N\cdot C_6H_4\cdot CHPh\cdot NH)_2CO$

thus analogous to the bathochromic shifts of the *y*-band brought about by methyl groups in the 3',3''- and 3',5',3'',5''-positions in Malachite Green.[3]

Substituents in the phenyl group of the hindered 2'-methyl and 2',2''-dimethyl derivative of Malachite Green produce spectral changes which are very similar to the changes which the same substituents produce in the parent dye (Table 1). Thus the values of $\Delta\lambda_{max.(x)}$ and $\Delta\lambda_{max.(y)}$ agree closely, and the values of $\varepsilon_{max.(x)}$ and $\varepsilon_{max.(y)}$ show the same pattern. In particular, the constancy of $\varepsilon_{max.(x)}$ (104,000—106,000) in the parent dye and its 4-methyl and 4-methoxy-derivative is repeated with the analogous 2'-methyl and 2',2''-dimethyl derivative ($\varepsilon_{max.(x)}$ 75,000 and 67,000—68,000, respectively), thereby confirming the previous deduction that these dyes exist wholly as the univalent, quinonoid cation in 98% acetic acid. Further, the unexpected increase in $\varepsilon_{max.(x)}$ shown by the 2-methyl derivative is repeated in the 2,2'-dimethyl and 2,2',2''-trimethyl derivative. The small bathochromic shift of the *x*-band shown by the first of these dyes contrasts with the small hypsochromic shifts shown by the *x*-bands of the other two, but the relevant comparison is between the corresponding 2- and 4-methyl derivatives in which case the spectral shifts are uniformly bathochromic to the extent of 6, 4, and 4 mμ, respectively.

Preparations.—The 2',2''-dimethyl derivative of leuco-Malachite Green is readily prepared from *NN*-dimethyl-*m*-toluidine and benzaldehyde, but the unsymmetrical 2'-methyl

TABLE 1. *Spectral data for derivatives of Malachite Green in* 98% *acetic acid.*

Subst.	$\lambda_{max.(x)}$ (mμ)	$\Delta\lambda_{max.(x)}$ (mμ)	$10^{-4}\varepsilon_x$	$\lambda_{max.(y)}$ (mμ)	$\Delta\lambda_{max.(y)}$ (mμ)	$10^{-4}\varepsilon_y$
None	621	—	10·4	427·5	—	2·0
2-Me	622·5	1·5	12·3	420	−7·5	1·5
4-Me	616·5	−4·5	10·6	437·5	10	2·5
4-OMe	608	−13	10·6	465	37·5	3·4
2'-Me	635	—	7·5	437·5	—	2·0
2,2'-Me_2	634	−1	8·4	431	−6·5	1·8
4,2'-Me_2	630	−5	7·5	447	9·5	2·5
4-OMe-2'-Me	620	−15	7·5	475	37·5	3·3
2',2''-Me_2	648	—	6·7	445	—	1·8
2,2',2''-Me_3	647·5	−0·5	7·4	440	−5	1·6
4,2',2''-Me_3	643·5	−4·5	6·8	475·5	12·5	2·2
4-OMe-2',2''-Me_2	633	−15	6·8	486	41	3·0

derivative requires the use of Yoshino's method[4] whereby *NN*-dimethylaniline is caused to react with benzaldehyde and urea to give the substituted urea (II) which with *NN*-dimethyl-*m*-toluidine gives the required leuco-compound. The use of substituted benzaldehydes in both of these reactions is satisfactory, but the 2',2''-dimethyl derivatives could not be oxidised to the dye with lead dioxide, chloranil, or lead tetra-acetate, despite

[3] Part II, *J.*, 1960, 3790.
[4] Yoshino, *Reports Govt. Chem. Ind. Res. Inst., Tokyo*, 1942, **37**, 95.

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the reported oxidation of analogous compounds on a commercial scale,[5] and the 2'-methyl derivative gave a coloured salt which could not be purified. The dye bases were therefore obtained directly by interaction of the appropriate aryl-lithium compound with the 2-methyl or 2,2'-dimethyl derivative of Michler's ketone, prepared from *NN*-dimethyl-*m*-toluidine and *p*-dimethylaminobenzoyl chloride or carbonyl chloride, respectively.[6] The dye bases were converted into the dyes in the 98% acetic acid used for the spectra determinations.

Experimental

4',4''-Bisdimethylamino-4,2'-dimethyltriphenylmethane.—A mixture of urea (3 g.), dimethylaniline (12·7 c.c.), *p*-tolualdehyde (11·8 c.c.), and 32% hydrochloric acid (10·4 c.c.) was stirred at room temperature for 20 hr. and then diluted with ethanol (200 c.c.), made alkaline with aqueous ammonia (*d* 0·88), and then refluxed until suspended material was completely crystalline, thereby yielding *NN-bis-(4-dimethylamino-4'-methyldiphenylmethyl)urea*, m. p. 234—235° (from pyridine) (Found: C, 78·4; H, 7·8; N, 11·2. $C_{33}H_{36}N_4O$ requires C, 78·2; H, 7·6; N, 11·1%). A mixture of this urea derivative (12·5 g.), *NN*-dimethyl-*m*-toluidine (7·2 c.c.), 32% hydrochloric acid (10·4 c.c.), and ethanol (40 c.c.) was stirred and refluxed for 24 hr. and then basified and poured into ethanol (100 c.c.), thereby yielding a solid which, twice crystallised from ethanol, gave *4',4''-bisdimethylamino-4,2'-dimethyltriphenylmethane* (15 g.), m. p. 130—132° (Found: C, 83·5; H, 8·4; N, 7·6. $C_{25}H_{30}N_2$ requires C, 83·8; H, 8·4; N, 7·8%).

4-Methoxy-2'-methyl-4',4''-bisdimethylaminotriphenylmethane.—By replacing benzaldehyde with *p*-anisaldehyde in the previous preparation, the *urea derivative*, m. p. 242—243° (from pyridine), was obtained (Found: C, 73·3; H, 7·0; N, 10·0. $C_{33}H_{38}N_4O_3$ requires C, 73·6; H, 7·1; N, 10·4%), and with *NN*-dimethyl-*m*-toluidine gave the *triphenylmethane derivative*, m. p. 114—115° (from ethanol) (Found: C, 80·0; H, 8·0; N, 7·4. $C_{25}H_{30}N_2O$ requires C, 80·2; H, 8·1; N, 7·5%).

4,4'-Bisdimethylamino-2'-methyltriphenylmethane.—Phenyl-lithium in ether, prepared from bromobenzene (3·14 g.), was added to 4,4'-bisdimethylamino-2-methylbenzophenone (1·41 g.) in ether (10 c.c.). The mixture was stirred at room temperature for 1 hr. and then poured into water. The ether was removed from the dried (Na_2SO_4) organic layer, yielding a gum which

Table 2. *Derivatives of Malachite Green base.*

			Found (%)			Required (%)		
Derivative	M. p.	Formula	C	H	N	C	H	N
2'-Me	146—147°	$C_{24}H_{28}N_2O$	80·0	7·8	7·6	80·0	7·8	7·8
2,2'-Me_2	150—151	$C_{25}H_{30}N_2O$	80·2	8·2	7·3	80·2	8·1	7·5
4,2'-Me_2	152—153	,,	80·0	7·8	7·3	80·2	8·1	7·5
2',2''-Me_2	142—143	,,	80·4	8·1	7·3	80·2	8·1	7·5
2,2',2''-Me_3	157—158	$C_{26}H_{32}N_2O$	80·3	8·4	7·2	80·4	8·3	7·2
4,2',2''-Me_3	164—165 (decomp.)	,,	80·6	8·5	7·0	80·4	8·3	7·2
4-OMe-2'-Me	152—153	$C_{25}H_{30}N_2O_2$	76·6	7·7	7·0	76·9	7·8	7·2
4-OMe-2',2''-Me_2 ...	175—176	$C_{26}H_{32}N_2O_2$	77·0	7·9	6·7	77·2	8·0	6·9

became crystalline in several hours and gave colourless *4,4'-bisdimethylamino-2'-methyltriphenylmethanol* (1·5 g.) (from ethanol). The other derivatives of triphenylmethanol given in Table 2 were prepared in a similar manner except that *p*-methoxyphenyl-lithium was prepared from butyl-lithium and *p*-bromoanisole by transmetallation.

One of us (G. H.) thanks the Department of Scientific and Industrial Research for a grant.

The University, Hull. [*Received, October 12th,* 1960.]

[5] Thorpe, "Dictionary of Applied Chemistry," Longman, Green and Co., London, 1954, Vol. XI, p. 705.

[6] Barker, Bride, and Stamp, *J.*, 1959, 3957.

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300. *Chemistry of the Higher Fungi. Part XII.* The Enzymic Decarboxylation of an αβ-Acetylenic Acid.*

By J. N. GARDNER, G. LOWE, and G. READ.

A cell-free extract from the Basidiomycete *Coprinus quadrifidus* has been shown to convert the hydroxy-acetylenic acid (I; R = CO_2H) into the alcohol (I; R = H) containing the free ethynyl group. The significance of this conversion is discussed in connexion with the occurrence of polyacetylenes containing an odd number of carbon atoms.

IT has been suggested that the free ethynyl group, which has been observed only in those fungal polyacetylenes with odd-numbered carbon chains,† is formed either by the decarboxylation of an αβ-acetylenic acid of even chain-length, or, perhaps less probably, by elimination of formaldehyde from the acetylenic alcohol.[1,2] In an attempt to gain experimental support for this hypothesis, *Coprinus quadrifidus* has been examined for an enzyme system capable of bringing about such a conversion. This organism was chosen because it has been shown to produce, in addition to C_{10} compounds, a series of closely related C_9 compounds containing the free ethynyl group. The substrate selected was the hydroxy-acid (I; R = CO_2H) since it can be readily prepared and detected spectroscopically and since the enediyne chromophore of the expected product (I; R = H) would also be easily detected.

Cell-free extracts obtained by crushing the mycelium of *C. quadrifidus* in a Hughes press[3] showed no interfering absorption in the ultraviolet region and had pH between 4 and 5. The extracts were adjusted to pH 7 before and after the addition of the substrate (I; R = CO_2H). The amount of polyacetylene present was estimated spectroscopically. It was found that the hydroxy-acid (I; R = CO_2H) was converted into a product with the

(I) $R{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}\overset{t}{C}H{=}CH{\cdot}CH_2OH$ $R{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ (II)

$HC{\equiv}C{\cdot}C{\equiv}C{\cdot}CH{=}C{=}CH{\cdot}\overset{c}{C}H{=}CH{\cdot}\overset{t}{C}H{=}CH{\cdot}CH_2{\cdot}CO_2H$ (III)

enediyne chromophore at approximately the same rate by equivalent concentrations of (*a*) blended mycelium, (*b*) crushed mycelial slurries, and (*c*) the supernatant solution from (*b*). The " cell solids " from (*b*) showed no activity. The cell-free extract (*c*) was used in the preparative experiments, and the enediyne produced after two days was isolated. It gave heptan-1-ol on hydrogenation and was oxidised by manganese dioxide to a diynenal. The infrared spectrum of the original product showed typical free ethynyl and *trans*-olefinic peaks, confirming its nature as the alcohol (I; R = H). In comparable small-scale experiments spectroscopic evidence was obtained which indicated that the related triynedicarboxylic acid (II; R = CO_2H) was similarly converted into the ethynyl-acid (II; R = H).

The isolation of the alcohol (I; R = H) in this experiment clearly supports the suggestion made from structural evidence,[1,2] that fungal metabolities containing the free ethynyl group are formed by cleavage at the terminal carbon atom of αβ-acetylenic metabolites. The absence of any intermediates such as the corresponding αβ-acetylenic aldehyde or alcohol and the common occurrence of decarboxylating enzymes in Nature renders the decarboxylation mechanism highly probable.

The enzyme system appears to be quite tolerant towards the gross structure of the

* Part XI, *J.*, 1960, 2257.

† One exception to this generalisation has recently been found. The biogenesis of this metabolite is being investigated.

[1] Jones, Pedler Lecture, 1959, *Proc. Chem. Soc.*, 1960, 199; Bu'Lock and Gregory, *Biochem. J.*, 1959, **72**, 322.

[2] Jones and Stephenson, *J.*, 1959, 2197.

[3] Hughes, *Brit. J. Exp. Path.*, 1951, **32**, 97.

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αβ-acetylenic acid as the products (I; R = H) and (II; R = H) are not natural metabolites of this organism. This enzyme system may therefore be of value in the synthesis of elaborate naturally occurring polyacetylenes such as mycomycin (III) in which the free ethynyl group represents a centre of considerable instability.

Experimental

For details of general experimental methods and conditions of culture growth see Part IX.[2]

8-Hydroxyoct-trans-6-*ene*-2,4-*diynoic acid* (I; R = CO_2H).—To a stirred solution of cuprous chloride (25 mg.) in 33% aqueous ethylamine (5·6 c.c.) was added an aqueous solution of 90% propiolic acid (0·89 g.). To this mixture in nitrogen at 15° *trans*-5-bromopent-2-en-4-yn-1-ol, prepared from *trans*-pent-2-en-4-yn-1-ol [4] (1·04 g.), was added during 10 min. Crystals of hydroxylamine hydrochloride were added as required to reduce any cupric ion formed. After being stirred for a further 10 min. the mixture was treated with potassium cyanide (0·25 g.), diluted with water (to 35 c.c.), and extracted with ether. The aqueous phase was acidified, and further ether-extraction gave the crude *hydroxy-acid* (I; R = CO_2H) (0·65 g., 67%). Crystallisation from ether–light petroleum afforded off-white prisms, slowly decomposing above 147° (Found: C, 63·6; H, 4·4. $C_8H_8O_3$ requires C, 64·0; H, 4·0%), $\lambda_{max.}$ (in EtOH) 3030 (ε 8050), 2850 (ε 11,350) 2700 (ε 9870), 2590 (ε 7900), 2495 (ε 7000), 2220 (ε 41,400), and 2165 Å (ε 44,000), $\nu_{max.}$ (in CS_2) 3340 (OH), 1650 (conjugated acid C=O stretching), and 940 cm.$^{-1}$ (*trans*-ethylenic hydrogen).

Cell-free Extract of C. quadrifidus.—After 15 days' growth, mycelium from six penicillin flasks of *C. quadrifidus* was washed with water, blended with 0·1M-phosphate buffer (pH 7·2) and crushed in a Hughes press.[3] On attaining room temperature the slurry obtained was centrifuged at 1800 ***g*** for 25 min. and the clear solution (*ca.* 100 c.c.) decanted from the " cell solids." The cell-free extract was used immediately.

trans-*Hept*-2-*en*-4,6-*diyn*-1-*ol* (I; R = H).—An aqueous solution (8 c.c.) of the acetylenic acid (I; R = CO_2H) (80 mg.) was added to the cell-free extract (90 c.c.), adjusted to pH 7·0 with saturated sodium hydrogen carbonate, and transferred to a sterile conical flask (500 c.c.) fitted with a sterile cotton-wool plug. After 48 hr. at 25° in the dark, when the spectrum of the ether extract of an acidified sample (1 c.c.) showed an optimum yield of the enediyne, the solution was diluted with water (100 c.c.) and extracted with ether. The dried ethereal solution was estimated spectroscopically to contain 25 mg. of enediyne. *The product* (I; R = H) was purified on a column of Woelm acidic alumina (1·5 × 6·0 cm.) and crystallised from hexane at −40° as fine colourless needles, m. p. 48—49°, rapidly becoming brown in light (Found: C, 77·0, 78·6; H, 6·1, 6·9. C_7H_8O requires C, 79·2; H, 5·7%), $\lambda_{max.}$ (in EtOH) 2785 (ε 10,600), 2640 (ε 13,800), 2500 (ε 9200), 2370 (ε 4900), 2260 (ε 2800), 2075 Å (ε 115,500), $\nu_{max.}$ (in CS_2) 3510 (OH), 3226 (≡CH), 951sh, and 942 cm.$^{-1}$ (*trans*-ethylenic hydrogen). Hydrogenation over 5% palladised charcoal gave heptan-1-ol, identified by vapour-phase chromatography. Oxidation with manganese dioxide in chloroform gave a product with typical diynenal spectrum, $\lambda_{max.}$ (in $CHCl_3$) 3040, 2860, 2700, and 2560 Å.

A control, prepared by heating a portion of the cell-free extract (2 c.c.) at 100° for 10 min., did not effect conversion of the hydroxy-acid (I; R = CO_2H) under the same conditions.

Enzymic Reaction of Acid (II; R = CO_2H).—The acetylenic dicarboxylic acid (II; R = CO_2H) (24 mg.; from *Merulius lacrymans* [5]) in a cell-free extract (50 c.c.; pH 5·9) from 27-day old mycelium of *C. quadrifidus* was incubated for 6 days at 22°. Extraction with ether did not remove residual substrate but gave an acidic fraction showing $\lambda_{max.}$ 2065 Å (in EtOH) (triyne) corresponding to *ca.* 2 mg. of the acetylenic acid (II; R = H). The methylated acid fraction showed a sharp band with $\nu_{max.}$ (in CS_2) 3300 cm.$^{-1}$ (C≡CH).

The authors thank Professor E. R. H. Jones, F.R.S., for his interest in this work, Dr. D. E. Hughes of the Medical Research Council Unit for Research in Cell Metabolism, Oxford, for helpful discussion and the use of apparatus, the Pressed Steel Company for a fellowship (G. R.), and the Ministry of Education of Northern Ireland for a post-graduate studentship (J. N. G.), also Mr. J. W. Keeping for the mycological work.

The Dyson Perrins Laboratory, Oxford. [*Received, October 20th*, 1960.]

[4] Chodkiewicz, *Ann. Chim.* (*France*), 1957, **2**, 852.
[5] Gardner, Jones, Leeming, and Stephenson, *J.*, 1960, 691.

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301. *Physicochemical Studies on Starches. Part XXIII.* Some Physical Properties of Floridean Starch and the Characterization of Structure-type of Branched α-1,4-Glucans.*

By C. T. Greenwood and J. Thomson.

Floridean starch has been isolated in granular and non-granular form from *Dilsea edulis*. Measurements were made on the polysaccharide of (i) the interaction with iodine, (ii) the variation of the sedimentation coefficient with concentration, and (iii) the limiting viscosity number. Comparable measurements are reported for rabbit-liver glycogen, the water-soluble polysaccharide from *Zea mays*, and the amylopectins from potato and malted-barley starch. A comparison of the results suggests that these physical measurements enable an unambiguous distinction to be made between amylopectin- and glycogen-type structures. On this basis, this sample of Floridean starch had a structure which was of the amylopectin-type. The weight-average molecular weight of the starch sample from light-scattering measurements was 7×10^8.

Although Floridean starch has been extensively studied,[1,2] it has not been established conclusively whether the polysaccharide is structurally more closely related to plant amylopectins or to animal glycogens. In this work, a sample of pure Floridean starch has been isolated in both granular and non-granular form, and some of its physical properties have been examined. These properties have been compared with those of other related branched α-1,4-glucans in order to investigate the relation between physical properties and structure-type.

Experimental

Isolation and Purification of the Floridean Starch.—(a) *Granular material.* A quantity of granular material (*ca.* 50 mg.) was isolated from the fronds of *Dilsea edulis* by extraction with 0·01M-mercuric chloride in a Blendor.[3] The extract was filtered through muslin, and the granular material obtained by centrifugation. The starch-product was deproteinized by repeated extraction of a saline suspension with toluene,[4] and then consisted of spherical, birefringent granules (diameter 5—10 μ), which stained violet with iodine (Found, N = 0·07%). The gelatinization temperature[3] was 45—47°. This procedure, normally used in starch extraction,[3] was not efficient, and other methods had to be used.

(b) *Non-granular starch.* Macerated fronds (*ca.* 250 g. wet-weight) were steeped in water (under toluene and at 4°) for 4 days to remove mucilaginous material. The fronds were then well washed with ethanol before they were covered with liquid ammonia in which they were left immersed for ½ hr. to disrupt cell walls. (This treatment has been shown to have no effect on the properties of the components of starch.[5]) The treated fronds were then extracted with water (1½ l.) at 98° for 1 hr. under nitrogen. Insoluble material was removed by centrifugation, calcium chloride (1 vol. of saturated solution) was added, and the mixture left at 2° for 24 hr. Precipitated calcium salts were removed by centrifugation, the solution was dialyzed, and the Floridean starch isolated by freeze-drying. The resultant product contained galactan (as shown by chromatographic examination of the hydrolysate). This was removed by three successive differential ultracentrifugations of an aqueous solution (0·5%) at 90,000 ***g*** (*i.e.*, at 40,000 r.p.m. in the preparative rotor of the Spinco model E ultracentrifuge). The sedimented product (0·75 g.) on hydrolysis gave only glucose on chromatographic examination, contained 98·5% of reducing sugar by alkaline ferricyanide titration, and had $[\alpha]_D^{18}$ +190° (*c* 0·1 in 0·1M-NaOH).

Characterization of the Floridean Starch.—Measurements were made of (i) the iodine-binding

* Part XXII, *Stärke*, 1960, **12**, 169.

[1] Fleming, Hirst, and Manners, *J.*, 1956, 2831, and references therein.
[2] Peat, Turvey, and Evans, *J.*, 1959, 3223, 3341.
[3] Banks and Greenwood, *Biochem. J.*, 1959, **73**, 237.
[4] Greenwood and Robertson, *J.*, 1954, 3769.
[5] Banks, Greenwood, and Thomson, *Makromol. Chem.*, 1959, **31**, 197.

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power,[6] (ii) the optical density of the glucan–iodine complex at various wavelengths,[3] (iii) the percentage conversion into maltose under the action of purified soya-bean β-amylase,[5] (iv) the average length of unit-chain by periodate oxidation in aqueous solution with sodium metaperiodate,[7] (v) the sedimentation coefficient of the glucan in 0·2M-potassium hydroxide,[8] (vi) the limiting viscosity number $[\eta]$ of the glucan in M-potassium hydroxide,[5] and (vii) the molecular weight of the glucan in 10^{-2}M-sodium chloride from light-scattering measurements [9] (these scattering measurements were kindly carried out by Dr. W. Banks and details of the results will be given elsewhere).

Results and Discussion

The isolation of granular material exhibiting birefringent properties strongly suggests that this amylaceous polysaccharide is, in fact, a starch. However, the crystallinity and degree of order in the granule must be radically different from that of a normal starch, as the gelatinization temperature (45—47°) is very much lower than is usual (60—98°, dependent on the source of starch [10]). This might be related to the different conditions of botanical environment.

The method of purification of the non-granular sample of Floridean starch by differential ultracentrifugation would remove any traces of short-chain amylose (cf. ref. 11). However, the supernatant liquor after ultracentrifugation did not give an iodine-stain, and it is not thought likely that any appreciable amount of linear material is present in the glucan.

The Table shows the properties of the non-granular sample of Floridean starch compared with those of a typical animal glycogen (from rabbit liver [9]) and a typical amylopectin (from potato starch [5]). Comparative results are also included for (i) the water-

Properties of Floridean starch and some other branched glucans.

Polysaccharide	Glycogen [9]	*Zea mays* polysaccharide [12]	Floridean starch	Malted barley amylopectin [13]	Potato amylopectin [5]
β-Amylolysis limit [a]	45 *	49	49	48 *	56
Average length of unit-chain.....	13·6	13 *	18·6	18·4 *	24
Average internal chain-length [b]	5	4·1	7	7·1 *	8·1
Limiting viscosity no. (with c in g./ml.)	7	7	160	146 *	200
$\lambda_{max.}$ of iodine-glucan complex (Å) ...	480	500	550	550	550

[a] Expressed as percentage conversion into maltose. [b] Calc. from {chain-length − [(chain-length × β-limit) + 2·5]}.
* Data taken from the reference at the head of the column.

soluble polysaccharide from sweet corn, *Zea mays*, which was thought to have a structure approximating to that of glycogen,[12] and (ii) the amylopectin from malted-barley starch, which differs from barley amylopectin only in the average length of external chain.[13]

The β-amylolysis results (49% conversion into maltose) are essentially similar to values of 46% and 42% reported earlier.[1,2] Our value of 18·6 anhydroglucose units for the average length of unit-chain of the *pure* glucan is similar to that of 15 reported by Peat and his co-workers.[2] A direct comparison with the results of Hirst and his co-workers [1] is not possible in view of the protein- and galactan-impurities in their samples; the protein-impurity in particular will interfere with the periodate oxidation (cf. ref. 14). Other comments on this estimation have been made by Peat and his co-workers.[2] The results of β-amylolysis experiments and chain-length estimations are not in themselves completely

[6] Anderson and Greenwood, *J.*, 1955, 3016.
[7] Potter and Hassid, *J. Amer. Chem. Soc.*, 1948, **70**, 3488.
[8] Bryce, Cowie, and Greenwood, *J. Polymer Sci.*, 1957, **25**, 251.
[9] Bryce, Greenwood, and Jones, *J.*, 1958, 3845.
[10] Greenwood and Thomson, unpublished experiments.
[11] Greenwood and Thomson, *Chem. and Ind.*, 1960, 1110.
[12] Greenwood and Das Gupta, *J.*, 1958, 703.
[13] Greenwood and Thomson, *J. Inst. Brewing*, 1959, 346.
[14] Anderson and Greenwood, *J. Sci. Food Agric.*, 1955, **6**, 587.

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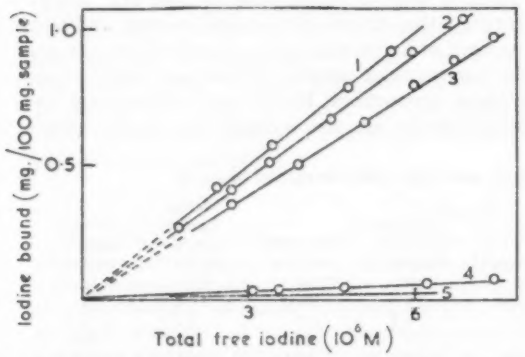
indicative of type-structure as quite wide variations can occur in any series of samples. It is to be noted, however, that Floridean starch and the malted-barley amylopectin have similar properties. When calculations are made of the average length of *internal* chains (on the assumption that β-amylase action ceases 2 or 3 glucose units away from a branch-point [15]), the glycogen and *Zea mays* polysaccharide examined appear to have internal chain-lengths of 4—5 units, whilst the other samples have values of 7—8. The significance of these differences is not yet known.

It is apparent, however, that there is a great difference between the value of the limiting viscosity numbers for the glycogen and *Zea mays* polysaccharide ($[\eta] = 7$) and those for the other samples ($[\eta] = 150$—200).

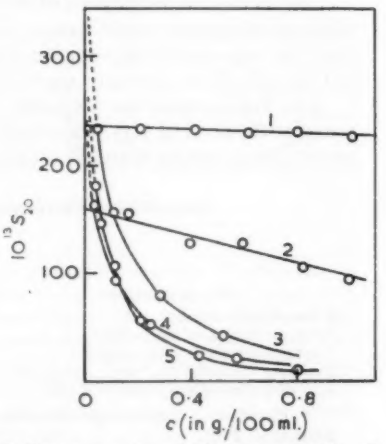
This difference is emphasized by the behaviour of the glucans towards iodine. Fig. 1 shows the potentiometric iodine-binding curves. (The curves for the amylopectins have

FIG. 1. *The iodine-binding power of branched α-1,4-glucans.*



1, *Potato amylopectin.* 2, *Malted-barley amylopectin.* 3, *Floridean starch.* 4, Zea mays *water-soluble polysaccharide.* 5, *Rabbit-liver glycogen.*[6]

FIG. 2. *Variation of sedimentation coefficient (S_{20}) with concentration (c) for branched α-1,4-glucans.*



1, Zea mays *water-soluble polysaccharide.* 2, *Rabbit-liver glycogen (extracted with trichloroacetic acid, see ref. 9).* 3, *Floridean starch.* 4, *Malted-barley amylopectin.* 5, *Potato amylopectin.*[6]

been corrected for any preferential uptake of iodine by linear material.[6]) The glycogen and *Zea mays* polysaccharide both have a similar, low iodine-binding power, whilst all the other glucans have a pronounced higher affinity for iodine. The Table shows that there is also a corresponding difference in the wavelength of maximum absorption of the iodine complex, although the difference is not so pronounced.

A further essential difference between branched-glucan structures is their behaviour on ultracentrifugation in alkaline solution; the sedimentation coefficient for glycogen-type materials is linear and relatively independent of concentration, whilst amylopectins are highly concentration-dependent.[8] Fig. 2 shows the results for the different glucans studied here, and again whilst the glycogen and *Zea mays* polysaccharide behave similarly, all the other samples are very concentration dependent.

The above evidence suggests that this sample of pure " Floridean starch " behaves as though it had an amylopectin-type rather than a glycogen-type structure. This conclusion is supported indirectly by the enzymic degradation experiments of Peat, Turvey,

[15] Peat, Whelan, and Thomas, *J.*, 1952, 4546.

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and Evans [2] who showed that their Floridean starch sample was degraded by R-enzyme. Further, its properties are remarkably similar to those of the amylopectin isolated from malted-barley starch.[13]

It is suggested that the results of comparative measurements of iodine-binding power, limiting viscosity number, and the concentration-dependence of the sedimentation coefficient can be used in conjunction unambiguously to classify the structure-type of a branched α-1,4-glucan. (The above results confirm our earlier suggestion [12] that the *Zea mays* polysaccharide has a glycogen-type structure.)

The weight-average molecular weight of this sample of Floridean starch was obtained from light-scattering experiments. Data for the intensity of the angular distribution of scattered light were evaluated by Zimm's method.[16] In 10^{-2}M-sodium chloride, the second virial coefficient for the sample was effectively zero. A molecular weight of 7×10^8 was found. This value is comparable to our results [17] for amylopectins. A detailed discussion of these results will be presented elsewhere.

The authors thank Prof. E. L. Hirst, C.B.E., F.R.S. for his valuable criticism and Dr. E. E. Percival for providing the sample of *Dilsea edulis*.

THE UNIVERSITY, EDINBURGH. [*Received, September 1st*, 1960.]

[16] Zimm, *J. Phys. Chem.*, 1948, **16**, 1093.
[17] Banks and Greenwood, unpublished results.

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302. *The Epoxide–Episulphide Transformation.*

By L. D. HALL, L. HOUGH, and R. A. PRITCHARD.

5,6-Dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-D-glucofuranose (XIV) has been prepared from 5,6-anhydro-1,2-*O*-isopropylidene-α-L-idofuranose (VIII), by reaction with thiourea. The α-L-*ido*-isomer (XII) was similarly prepared from 5,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose (V). Cyclisation of 6-acetylthio-6-deoxy-1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-glucofuranose (XI) with sodium methoxide gave the L-*ido*-episulphide, thus confirming that the epoxide–episulphide transformation proceeds with inversion. Desulphurisation of the above 5,6-episulphides and their 5,6-trithiocarbonates afforded 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (XIII), which was identical with that prepared by hydrogenation of 5,6-didehydro-5,6-dideoxy 1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (IX). Opening of the 5,6-episulphide ring by acid and by alkali is discussed.

INTEREST in 5-deoxy-5-mercapto-D-glucose and the possibility that intramolecular reaction of the carbonyl group with the thiol group would give a six-membered cyclic hemiacetal analogous to the pyranose forms of D-glucose, caused us to investigate the preparation of 5,6-dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-D-glucofuranose (XIV) and the corresponding L-*ido*-isomer (XII), and their subsequent ring opening.

It is well known that an epoxide can be converted, probably with inversion, into an episulphide [1] by treatment with an alkali-metal thiocyanate or a thiourea. Consequently the preparation of 5,6-anhydro-D-glucose (V) and 5,6-anhydro-L-idose (VIII) derivatives from 6-*O*-tosyl (I) and 6-*O*-benzoyl-5-*O*-tosyl (IV) derivatives of 1,2-*O*-isopropylidene-α-D-glucofuranose respectively was examined. Although the precautions suggested by Tipson [2] were observed attempts to prepare the 5-*O*-tosyl (IV) and the 5-*O*-methanesulphonyl derivative of 6-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose by the method

[1] (*a*) Dachlauer and Jackel, G.P. 636,708/1936; (*b*) Culvenor, Davies, and Pausacker, *J.*, 1946, 1050; (*c*) Snyder, Stewart, and Ziegler, *J. Amer. Chem. Soc.*, 1947, **69**, 2672; (*d*) Culvenor, Davies, and Heath, *J.*, 1949, 278; (*e*) Goodman, Benitez, and Baker, *J. Amer. Chem. Soc.*, 1958, **80**, 1680.
[2] Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 107.

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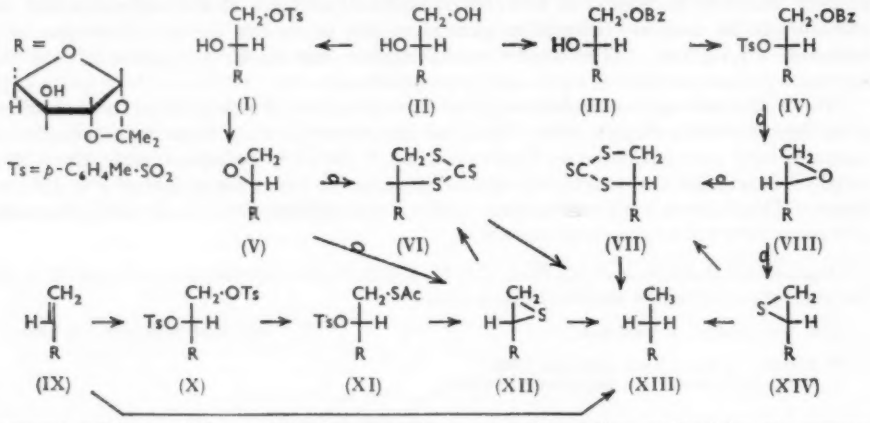
of Ohle and Dickhauser [3] were unsuccessful, almost quantitative recoveries of starting material being obtained. The sulphonylation was successfully achieved by a method communicated to us by Professor L. von Vargha,[4] the essential points being the extreme concentration of the reaction solution, the use of solid toluene-*p*-sulphonyl chloride, and the



extreme mildness of the purification procedure. An alternative method for the preparation of the 5-*O*-tosyl derivative (IV) was suggested [5] by the successful reduction of 1,2-*O*-isopropylidene-5-*O*-methyl-α-D-glucofuranurono-6 ⟶ 3-lactone with lithium aluminium hydride to 1,2-*O*-isopropylidene-5-*O*-methyl-α-D-glucofuranose. 1,2-*O*-Isopropylidene-5-*O*-tosyl-α-D-glucofuranurono-6 ⟶ 3-lactone was prepared from the easily accessible D-glucofuranurono-6 ⟶ 3-lactone, but this derivative, and the corresponding 5-*O*-methanesulphonyl derivative, resisted reduction by a variety of reagents, including potassium and lithium borohydride, lithium aluminium hydride, and hydrogen in the presence of catalysts. This inactivity was probably due to a combination of steric hindrance, which inhibits the approach of the attaching group (*e.g.*, BH_4^-), and electronic factors which decrease the cationoid character of the carbonyl-carbon atom.

The epoxide–episulphide transformation was then studied by treatment of the 5,6-anhydro-compounds (V and VIII) with potassium thiocyanate, or with thiourea under varying conditions (Table 1). At first, reaction solutions containing 10% or more of the 5,6-anhydro-compound (V) were used, but this resulted in low yields of the episulphide (XII), and the formation of a gum, which was presumed to be polymeric since it was insoluble in both water and chloroform. It was shown that this polymerisation was due solely to a concentration effect, and not to either photosensitivity or aerial oxidation of the product: increased yields (>75%) of episulphides were obtained, with no polymerisation, when the concentration anhydro-compound was reduced to ~3%. It is noteworthy that Culvenor, Davies, and Savige [6] found that polymerisation of ethylene sulphides cannot be checked by ordinary antioxidants such as quinol.

Desulphurisation of the episulphides with Raney nickel gave 5,6-dideoxy-1,2-*O*-isopropylidene-D-*xylo*-hexofuranose (XIII) in both cases (see below), proving that they were isomeric 5,6-episulphides and that no migration to give, for example, a 3,6-episulphide had occurred.

Previous evidence [6,7] suggested that the reaction is accompanied by Walden inversion,

[3] Ohle and Dickhauser, *Ber.*, 1925, **58**, 2593.
[4] von Vargha, personal communication.
[5] Jones, *Canad. J. Chem.*, 1956, **34**, 310.
[6] Culvenor, Davies, and Savige, *J.*, 1952, 4480.
[7] Ettlinger, *J. Amer. Chem. Soc.*, 1950, **72**, 4792; van Tamelen, *ibid.*, 1951, **73**, 3444; Goodman and Baker, *ibid.*, 1959, **81**, 4924; Price and Kirk, *ibid.*, 1953, **75**, 2396; Bordwell and Andersen, *ibid.*, 1953, **75**, 4959; Reynolds, *ibid.*, 1957, **79**, 4951.

TABLE 1. *The epoxide–episulphide transformation.*

Starting isomer	Epoxide (g.)	Concn. (%)	Reaction time (hr.)	Temp.	Reagent	Yield (%)
D-*gluco*- (V)	0·2	10	1	50°	KCNS	5
	3·1	15	1	50	,,	30
	0·5	10	22	20	$CS(NH_2)_2$	33
	0·2	2·5	8	20	,,	78
	9·5	3·0	24	20	,,	75
L-*ido*- (VIII)	0·2	2·5	48	20	,,	78
	1·0	2·5	48	27	,,	79
	3·4	2·5	48	27	,,	76

but confirmation of this for the epoxide–episulphide transformation was felt to be desirable. Cyclisation of 3,5-di-*O*-acetyl-6-acetylthio-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose to the L-*ido*-episulphide (XII) was attempted, but in agreement with Creighton and Owen [8] neither methanolic sodium methoxide nor aqueous sodium hydroxide was satisfactory. Since the toluenesulphonyloxy-group is a better " departer " than the acetoxy-group, cyclisation of 6-acetylthio-6-deoxy-1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-glucofuranose (XI) was likely to be more successful. Replacement of the primary toluene-*p*-sulphonyloxy-group in 1,2-*O*-isopropylidene-5,6-di-*O*-tosyl-α-D-glucofuranose (X) by treatment [9] with potassium thiolacetate gave the acetylthio-derivative (XI) in 60% yield. Treatment of this compound with methanolic sodium methoxide gave an 89% yield of 5,6-dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-L-idofuranose (XII), which was identical with that obtained by the reaction of thiourea and potassium thiocyanate with 5,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose, thus providing unequivocal proof that inversion had occurred during the epoxide–episulphide transformation. This confirms the observations of Creighton and Owen [8] who recently described a similar series of reactions.

McSweeney and Wiggins [10] prepared a crystalline 5,6-trithiocarbonate (VI) by heating a mixture of carbon disulphide, potassium hydroxide, and 5,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose in methanol and characterised the product by desulphurisation with Raney nickel to 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (XIII). In agreement with the suggestion [1b] that an episulphide (XII) acts as an intermediate in the formation of the trithiocarbonate, 5,6-dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-L-idofuranose gave, with these reagents at *room temperature*, a high yield of the same trithiocarbonate. Since there must be an overall inversion of configuration at $C_{(5)}$, the product is 5,6-dideoxy-5,6-dithio-1,2-*O*-isopropylidene-α-L-idofuranose 5,6-trithiocarbonate (VI). This conclusion was reached independently by Creighton and Owen.[8] When this reaction was applied to the isomeric 5,6-anhydro- (VIII) and 5,6-episulphide (XIV) derivatives, similar results were obtained although the yellow 5,6-trithiocarbonate (VII) was contaminated with a colourless impurity which could not be removed. Culvenor, Davies, and Pausacker [1b] also obtained from cyclohexene oxide a trithiocarbonate which contained an unidentified white impurity.

Desulphurisation of each of the episulphides (XII, XIV), and the trithiocarbonates (VI, VII), gave the same product, namely, 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (XIII). McSweeney and Wiggins [10] also obtained this compound (m. p. 78°, $[\alpha]_D$ −31·4°) by reductive desulphurisation of the L-*ido*-trithiocarbonate (VI), but offered no structural proof other than the method of preparation. English and Levy,[11] however, obtained by the catalytic hydrogenation of 3-*O*-benzyl-5,6-didehydro-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*hexofuranose a product which had m. p. 79·0—79·6° $[\alpha]_D$ −21·9°, and gave a depression of m. p. on admixture with McSweeney and Wiggins's compound. They then established the structure of their isopropylidene derivative by hydrolysis to the free

[8] Creighton and Owen, *J.*, 1960, 1024.
[9] Chapman and Owen, *J.*, 1950, 579.
[10] McSweeney and Wiggins, *Nature*, 1951, **168**, 874.
[11] English and Levy, *J. Amer. Chem. Soc.*, 1956, **78**, 2846.

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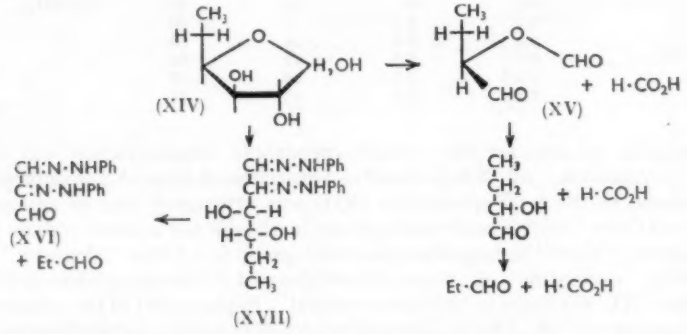
sugar and subsequent periodate oxidation, in which 3 mol. of oxidant were consumed with the formation of propionaldehyde. English and Levy suggested that McSweeney and Wiggins's compound might be an isomer, formed by some rearrangement during preparation of the trithiocarbonate.

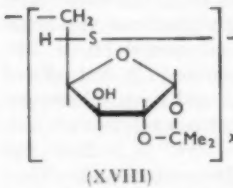


A specimen of English and Levy's dideoxy-compound (XIII), kindly provided by Professor J. English, gave no depression in m. p. with our specimen prepared by the method of McSweeney and Wiggins. Identity of these samples was confirmed by comparison with another specimen prepared by the hydrogenation of 5,6-didehydro-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (IX). [The compound (IX) was obtained crystalline by treating 1,2-*O*-isopropylidene-5,6-di-*O*-tosyl-α-D-glucofuranose with sodium iodide, by a modification of Oldham and Rutherford's method.[12]]

Acid-hydrolysis of the isopropylidene derivative (XIII) gave a reducing sugar (XIV) which rapidly (1 hr.) consumed 2 mol. of periodate, giving 1 mol. of formic acid, and then slowly (24 hr.) a third mol., liberating a further 2 mol. of acid. Propionaldehyde was isolated and characterised as its 2,4-dinitrophenylhydrazone. These results are consistent with the oxidation of a 5,6-dideoxyhexose in the furanose form (XIV) to a relatively stable intermediary formyl ester of 3,4-dideoxy-D-*glycero*-tetrose (XV), in agreement with the previous findings [13] that the stability of a formyl ester is related to the electrophilic character of the adjacent groups.

The structure of the 5,6-dideoxy-D-*xylo*-hexose (XIV) was verified by oxidising its phenylosazone (XVII) with sodium metaperiodate: mesoxalaldehyde 1,2-bisphenylhydrazone (XVI) was obtained [14] in high yield.

Attempted ring opening of the 5,6-episulphides by 0·1N-sodium hydroxide at room temperature yielded polymeric material which was insoluble in chloroform and in water. Culvenor, Davies, and Heath [14] noted that the powerful polymerising action of sodium hydroxide and other strongly alkaline reagents was due to the opening of an episulphide ring to give the sodium derivative of the thiol, which then attacked another episulphide ring, thus rapidly giving a chain polymer. As expected from steric considerations, the tendency to polymerise was greater when the side-chain was small, and our findings are in agreement with this, since the 5,6-episulphides required *ca.* 15 hr. for complete polymerisation. Polymerisation resulted in a shift of the characteristic sulphide absorption from 206 to 230 mμ, without the formation of disulphide absorption at 300 mμ, and at no stage of the reaction was a positive thiol test obtained. This evidence, and the isolation of 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose in good



[12] Oldham and Rutherford, *J. Amer. Chem. Soc.*, 1932, **54**, 366.
[13] Hough, Taylor, Thomas, and Woods, *J.*, 1958, 1212.
[14] Hough, Powell, and Woods, *J.*, 1956, 4799.

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yield on desulphurisation of the polymer, was in agreement with a structure containing a repeating unit of 5,6-dideoxy-1,2-*O*-isopropylidene-*hexo*-furanose 5(6')-sulphide (XVIII).

Acid-hydrolysis of the L-*ido*-episulphide (XII) with N-sulphuric acid at room temperature involved a complex change in rotation, a maximum value (+34°) being rapidly attained in 2½ hr. followed by a gradual decrease (to −6° in 48 hr.). The episulphide was shown by paper chromatography to give at least four components, the proportions varying with the reaction time. After partial hydrolysis (24 hr.), one fraction was separated on a cellulose column and identified as 5,6-dideoxy-5,6-epithio-L-idofuranose ($[\alpha]_D$ +33·3°). This reducing sugar was the initial product of the hydrolysis, its formation corresponding to the initial rapid increase in the optical rotation. Treatment of this compound with acid yielded a mixture containing the other three products of the original hydrolysate, which will be described later.

Experimental

Concentrations were carried out under reduced pressure. M. p.s were determined on a Kofler microscope stage. Optical rotations were determined for $CHCl_3$ solutions at 25° ± 1°. Paper chromatography was carried out on Whatman No. 1 filter paper by the descending method, with butan-1-ol–pyridine–water (10 : 3 : 3 v/v) as solvent, and rates of movement are quoted with reference to 2,3,4,6-tetra-*O*-methyl-D-glucose (R_G). Acylations were performed under rigorously anhydrous conditions, in apparatus dried at 100° and with purified reagents.

5,6-*Dideoxy*-5,6-*epithio*-1,2-O-*isopropylidene*-α-L-*idofuranose* (XII).—(a) *From* 5,6-*anhydro*-1,2-O-*isopropylidene*-α-D-*glucofuranose* (V). A solution of the anhydro-compound [15] (9·56 g.) and thiourea (3·6 g., 1·5 mol.) in methanol (250 ml.) was kept at room temperature, and the change in optical rotation observed: $[\alpha]_D$ −40° ⟶ −30° (constant; 10 hr.). After 24 hr. ice-water (350 ml.) was added, methanol removed by evaporation at room temperature, and the aqueous solution extracted several times with chloroform. The combined extracts were dried (Na_2SO_4) and concentrated, affording crystals, m. p. 162—165° (sublimes). Recrystallisation from light petroleum (b. p. 40—60°) gave the epithio-compound (XII) as needles (7·75 g., 75%), m. p. 167—169°, $[\alpha]_D$ −17·5° (*c* 3·1), sublimes at 80—130° (bath)/5 × 10^{-3} mm. (Found: C, 49·7; H, 6·6; S, 14·3. Calc. for $C_9H_{14}O_4S$: C, 49·5; H, 6·5; S, 14·7%). Paper chromatography gave a single white-centred spot (R_G 0·67; R_F 0·85) when sprayed with ammoniacal silver nitrate {lit.,[8] m. p. 164—165°, $[\alpha]_D$ −16° (*c*, 5)}. In one experiment the aqueous solution remaining after chloroform-extraction was concentrated to yield urea (66%), m. p. and mixed m. p. 126°.

(b) *From* 6-*acetylthio*-6-*deoxy*-1,2-O-*isopropylidene*-5-O-*tosyl*-α-D-*glucofuranose* (XI). Methanolic sodium methoxide [from sodium (0·102 g.) in dry methanol (5 ml.)] was added to a solution of the acetylthio-compound (1·87 g.) in chloroform (59 ml.) at −10° under anhydrous conditions. The resultant colloidal mass was shaken at −10° for 30 min., water (20 ml.) added, the chloroform layer removed, and the aqueous layer extracted with chloroform (3 × 10 ml.). The combined chloroform extracts were washed with water (3 × 30 ml.), dried ($CaSO_4$), and concentrated to a colourless solid (1·00 g.). This crystallised from chloroform–light petroleum (b. p. 60—80°) as needles of the epithio-compound (XII) (0·86 g., 89%), m. p. 166—168°. Further recrystallisation gave material of m. p. 169—170° (undepressed on admixture with the episulphide described above), $[\alpha]_D$ −17·6° (*c* 1·4). This product with acetic anhydride and pyridine gave 3-O-*acetyl*-5,6-*dideoxy*-5,6-*epithio*-1,2-O-*isopropylidene*-α-L-*idofuranose* as needles, m. p. 77—78° (sublimes) (Found: C, 51·2; H, 6·3; S, 10·5; Ac, 14·1. $C_{11}H_{16}O_5S$ requires C, 50·8; H, 6·2; S, 12·3; Ac, 16·5%).

1,2-O-*Isopropylidene*-5,6-*di*-O-*tosyl*-α-D-*glucofuranose* (X).—The ditosyl compound was prepared in 20% yield by the action of toluene-*p*-sulphonyl chloride on 1,2-*O*-isopropylidene-α-D-glucofuranose (method of Ohle and Dickhauser [16]). The yield was improved by the following procedure. 1,2-*O*-Isopropylidene-α-D-glucofuranose (10 g.) was mixed with benzene (40 ml.) and pyridine (20 ml.), and a solution of toluene-*p*-sulphonyl chloride (17·5 g., 2·01 mol.) in chloroform (35 ml.) was added at 0°. The yellow mixture was kept at room temperature for

[15] Mehltretter, Alexander, Mellies, and Rist, *J. Amer. Chem. Soc.*, 1951, **73**, 2424; Meyer and Reichstein, *Helv. Chim. Acta*, 1946, **29**, 139; Ohle and Vargha, *Ber.*, 1929, **62**, 2435.

[16] Ohle and Dickhauser, *Ber.*, 1925, **58**, 2593.

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24 hr., then cooled to 0°, and water (10 ml.) was added dropwise, followed 30 min. later by 2N-hydrochloric acid (100 ml.). The aqueous layer was extracted with chloroform (2 × 150 ml.), the combined extracts were washed successively with 2N-hydrochloric acid (2 × 100 ml.), N-sodium hydrogen carbonate (100 ml.), and water (2 × 100 ml.), and dried (Na_2SO_4). Concentration produced a pale-yellow syrup which crystallised from ethanol as colourless needles (10 g.). Further crystallisation from ethanol gave the ditosyl compound (X) (9·3 g., 40%), m. p. 161—162° $[\alpha]_D$ −6·85° (*c* 2·7) (Found: C, 52·3; H, 5·65. Calc. for $C_{23}H_{28}O_{10}S_2$: C, 52·25; H, 5·35%) (lit.,[16] m. p. 160°, $[\alpha]_D$ −6·37°).

6-*Acetylthio*-6-*deoxy*-1,2-O-*isopropylidene*-5-O-*tosyl*-α-D-*glucofuranose* (XI).—The ditosyl compound (X) (1·865 g.) and potassium thiolacetate (0·861 g.) in ethyl methyl ketone (40 ml.) were heated under reflux for 1 hr. The mixture was concentrated to dryness, the residue fractionated between water (10 ml.) and chloroform (30 ml.), and the chloroform layer separated. The aqueous layer was extracted with chloroform (2 × 15 ml.), and the combined chloroform extracts were washed with water (20 ml.), dried ($CaSO_4$), and on concentration gave a yellow solid (1·558 g.). This was dissolved in methanol and decolorised (charcoal), and on evaporation the *acetylthio-compound* (XI) was obtained as needles (0·90 g., 60%), m. p. 139—140°, $[\alpha]_D$ +4·32° (*c* 1·5), $\nu_{max.}$ 1500, 1600 (Ph), 1693 (*S*-Ac), 3430 (OH) (Found: C, 50·15; H, 5·55. $C_{16}H_{24}O_8S_2$ requires C, 50·0; H, 5·6%).

6-O-*Benzoyl*-1,2-O-*isopropylidene*-5-O-*tosyl*-α-D-*glucofuranose*[4] (IV).—Toluene-*p*-sulphonyl chloride (33 g.) was added during 1 hr. to a stirred solution of the benzoyl compound[17] (VII) (50 g.) in pyridine (250 ml.) at 0° under rigorously anhydrous conditions. The mixture was kept at room temperature for 24 hr., the pyridine removed by distillation, and the residue dissolved in ether (200 ml.)–water (150 ml.) and filtered. The ether extract was washed with water, dried (Na_2SO_4), and evaporated, giving a syrup which crystallised from ethanol (70 ml.) as the tosyl derivative (IV) (15 g., 20%), m. p. 143—144° (Found: C, 57·8; H, 5·6. Calc. for $C_{23}H_{26}O_9S$: C, 57·7; H, 5·5%) (lit.,[16] m. p. 142°).

5,6-*Dideoxy*-5,6-*epithio*-1,2-O-*isopropylidene*-α-D-*glucofuranose* (XIV).—This compound was prepared from the anhydro-compound (Mehltretter *et al.*[15]) (VIII) by the method described above for the L-*ido*-isomer, the mixture taking 48 hr. to reach constant optical rotation. The crude crystalline compound had m. p. 138—140° (sublimes) and was purified by sublimation at 80—130° (bath)/5 × 10^{-3} mm., to give the *compound* (XIV) as needles (78·5%), m. p. 139—142°, $[\alpha]_D$ −76·2° (*c* 1·9) (Found: C, 49·5; H, 6·8; S, 14·65. $C_9H_{14}O_4S$ requires C, 49·5; H, 6·5; S, 14·7%).

The 5,6-episulphides give brilliant yellow solutions in concentrated sulphuric acid; no similar behaviour was observed with any of the precursors of either isomer.

5,6-*Dideoxy*-1,2-O-*isopropylidene*-5,6-*dimercapto*-α-L-*idofuranose* 5,6-*Trithiocarbonate* (VI).—(a) *From* 5,6-*anhydro*-1,2-O-*isopropylidene*-α-D-*glucofuranose*. A solution of the anhydro-compound (V) (0·10 g.), potassium hydroxide (0·07 g.), and carbon disulphide (0·1 ml.) in methanol (5 ml.) was heated under reflux for 2 hr., then poured into ice-water, giving the xanthate (VI) (0·095 g., 70%), m. p. 177—178°. After recrystallisation from aqueous ethanol this had m. p. 178—179°, $[\alpha]_D$ +2° (*c* 1·08), $\lambda_{max.}$ 316 mμ (ε 14,000) (Found: C, 40·6; H, 5·0. Calc. for $C_{10}H_{14}O_4S_3$: C, 40·8; H, 4·8%).

(b) *From* 5,6-*dideoxy*-5,6-*epithio*-1,2-O-*isopropylidene*-α-L-*idofuranose*. A mixture of this sulphide (0·019 g.) with potassium hydroxide (0·018 g.) and carbon disulphide (0·02 ml.) in methanol (10 ml.) was kept at room temperature for 24 hr., then poured into ice-water, and the crystalline product collected and purified as before (0·0192 g., 75%), m. p. and mixed m. p. 178—179° (lit.,[10] m. p. 179·5—180·5°).

5,6-*Dideoxy*-1,2-O-*isopropylidene*-5,6-*dimercapto*-α-D-*glucofuranose* 5,6-*Trithiocarbonate* (VII).—Attempts to prepare this compound from 5,6-anhydro-1,2-*O*-isopropylidene-α-L-idofuranose and 5,6-dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-D-glucofuranose, using the methods (a) and (b) described for the L-*ido*-isomer gave an impure product ($[\alpha]_D$ of samples varied from −100° to −250°, whilst the m. p. varied between 198° and 210°). It ran on chromatograms with the L-*ido*-isomer and gave a white spot (R_G 0·69) on a brown background with the silver nitrate spray. It had a characteristic trithiocarbonate absorption in the ultraviolet region (λ_{max} 316 mμ).

5,6-*Dideoxy*-1,2-O-*isopropylidene*-α-D-xylo-*hexofuranose* (XIII).—5,6-Dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-L-idofuranose (0·60 g.) and Raney nickel (*ca.* 2 g.) were heated under

[17] Ohle, *Ber.*, 1924, **57**, 403.

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reflux in ethanol (30 ml.) for 3 hr. Filtration and concentration gave crystals which recrystallised from light petroleum (b. p. 60—80°) as needles (0·370 g., 72%), m. p. 77—78° (sublimes), mixed m. p. with an independent sample [11] 77—79°, $[\alpha]_D$ −26·3° (*c* 3·08) (Found: C, 57·7; H, 8·3. Calc. for $C_9H_{16}O_4$: C, 57·4; H, 8·6%) (lit.,[10,11,13] m. p. 78·7—79·5°, $[\alpha]_D$ −21·9°; $[\alpha]_D$ −31·4°).

Similar treatment of 5,6-dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-D-glucofuranose, 5,6-dideoxy-1,2-*O*-isopropylidene-5,6-dimercapto-α-L-idofuranose 5,6-trithiocarbonate (VI), and 5,6-dideoxy-1,2-*O*-isopropylidene-5,6-dimercapto-α-D-glucofuranose 5,6-trithiocarbonate (VII) gave products identical with (XIII) in m. p., mixed m. p., opical rotation, and *X*-ray powder photographs.

5,6-*Didehydro*-5,6-*dideoxy*-1,2-O-*isopropylidene*-α-D-xylo-*hexofuranose* (IX).—1,2-*O*-Isopropylidene-5,6-di-*O*-tosyl-α-D-glucofuranose (1·70 g.) and sodium iodide (3·0 g.) were heated under reflux for 1½ hr., in dry ethyl methyl ketone (50 ml.). The precipitated sodium toluene-*p*-sulphonate was filtered off, washed with ethyl methyl ketone, dried at 70°, and weighed (1·24 g., 100%). Concentration of the combined filtrates produced a brown residue which was fractionated between aqueous sodium thiosulphate (5 g. in 50 ml.) and chloroform (30 ml.). The aqueous layer was then extracted with chloroform (2 × 30 ml.), and the combined chloroform extracts were washed with water, and dried ($CaSO_4$). Concentration produced a yellow syrup, a methanolic solution of which was decolorised with charcoal and concentrated to a solid (0·541 g., 92·5%), m. p. 59—63°, which contained no sulphur (Lassaigne test). Sublimation at 70° (bath)/10^{-3} mm. afforded needles of 5,6-*didehydro*-5,6-*dideoxy*-1,2-O-*isopropylidene*-α-D-xylo-*hexofuranose* (0·50 g., 85%), m. p. 61—65°, $[\alpha]_D$ −51·5° (*c* 1·1), $\nu_{max.}$ 920, 1420, 1644, 1884, 3030, 3080 (monosubstituted ethylene derivative), 3430 (OH) (Found: C, 57·95; H, 7·8. $C_9H_{14}O_4$ requires C, 58·0; H, 7·6%).

5,6-*Dideoxy*-1,2-O-*isopropylidene*-α-D-xylo-*hexofuranose* (XIII).—The unsaturated derivative (IX) (0·1098 g.) was hydrogenated at atmospheric pressure in absolute ethanol (20 ml.), with 10% palladium–charcoal (0·144 g.) (uptake 25·7 ml. in 1 hr., 1·03 mol.). The catalyst was filtered off and washed with ethanol, and the combined filtrates were concentrated, affording crystals (0·199 g., 99·5%), m. p. 60—64°. Recrystallisation from light petroleum (b. p. 60—80°) afforded 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose as plates (0·1909 g., 95%), m. p. 60—64·5°, $[\alpha]_D$ −22·5° (*c* 1·1). The plates changed to needles at room temperature, and the m. p. increased to 70—74° (12 days). A sample purified by vacuum-sublimation at 70° (bath)/10^{-3} mm. had m. p. 77—78°, and mixed m. p. with sample prepared by English and Levy,[11] 77—79°.

5,6-*Dideoxy*-D-xylo-*hexofuranose* (XIV).—5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (0·093 g.) was heated in 0·1N-hydrochloric acid (10 ml.) at 95—100° to constant optical rotation (0·5 hr.). The solution was neutralised with Amberlite resin IR-4B(OH^-), and concentrated to a syrup, which showed a single spot (R_G 0·59) on paper chromatograms with both the silver nitrate and the *p*-anisidine hydrochloride sprays.[19]

Periodate Oxidation of 5,6-*Dideoxy*-D-xylo-*hexofuranose*.—5,6-Dideoxy-D-*xylo*-hexofuranose (0·028 g.) was dissolved in 0·09M-sodium metaperiodate (100 ml.) and stored in the dark alongside a blank solution containing no sugar derivative. At intervals, aliquot portions (5 ml.) were added to a mixture of phosphate buffer (pH 6·9; 15 ml.) and 20% potassium iodide solution (2 ml.), and the liberated iodine was titrated with 0·1N-sodium thiosulphate (starch indicator). Aliquot portions (5 ml.) were also taken for formic acid estimation, mixed with ethylene glycol (2 ml.), left for 15 min., and titrated potentiometrically to pH 6·28.[20]

The " fugitive end-point " encountered during these titrations indicated the presence of a formyl ester in solution: [21]

Time (hr.)	1	2½	4½	24
Periodate uptake (mol.)	2·2	2·3	2·4	2·72
Formic acid (mol.)	1·45	1·67	1·90	2·56

The remaining periodate oxidation solution was extracted several times with ether, and the combined ether extracts were treated with Brady's reagent (1·5 ml.). Concentration gave a

[18] Jones and Thompson, *Canad. J. Chem.*, 1957, **35**, 955.
[19] Hough, Jones, and Wadman, *J.*, 1949, 2511; 1950, 1702.
[20] Anderson, Greenwood, and Hirst, *J.*, 1955, 225.
[21] Morrison, Kuyper, and Orten, *J. Amer. Chem. Soc.*, 1953, **75**, 1502.

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mixture of crystals which were dissolved in chloroform and fractionated on a column of bentonite–kieselguhr,[22] with ethanol–chloroform (1 : 5 v/v), to give propionaldehyde 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 154°.

5,6-*Dideoxy*-D-threo-*hexosazone*.[23]—A mixture of 5,6-dideoxy-D-*xylo*-hexofuranose (0·05 g.), water (1 ml.), acetic acid (0·5 ml.), and phenylhydrazine (0·22 ml.) was heated at 95—100° for 45 min. The crystalline product was filtered off, washed with cold water and cold benzene, and dried, giving the phenylosazone (XVII) as yellow needles (0·055 g.), m. p. 163—165°.

Periodate Oxidation of 5,6-*Dideoxy*-D-threo-*hexosazone*.—Without further purification, the osazone (XVII) was dissolved in 70% ethanol (10 ml.), mixed with 0·3M-sodium metaperiodate (2 ml.), and left at room temperature for 2 hr. The bright orange precipitate was collected on a sintered-glass filter, washed with water, and dried. Recrystallisation from ethanol–water gave mesoxalaldehyde 1,2-bisphenylhydrazone (XVI) (0·068 g.), m. p. and mixed m. p. 195—196°. The ultraviolet absorption of this product was identical with that of an authentic specimen, prepared by periodate oxidation of D-*arabo*-hexose phenylosazone.

TABLE 2. *Attempted reduction of lactone derivatives.*

Reagent nature	mol.	Solvent	Time (hr.)	Temp.	Product *	Ref.
KBH_4	1·8	Aq. dioxan	18	20°	Acid syrup	25
$LiBH_4$	5	Dioxan	24	20	—	26
$LiBH_4$	4	Tetrahydrofuran	24	50	—	
$LiAlH_4$	1·1	Ether	1	35	—	
$LiAlH_4$	7	Tetrahydrofuran	2½	70	Acid syrup	
KBH_4–NaOMe	2	Methanol	24	20	,,	27
KBH_4–H_3BO_3	1·1	Methylcellosolve–water	4	20	,,	
KBH_4–HOAc	5	,, ,,	6	20	,,	28
H_2–Pt_2O (200 lb./in.²)			7	100	,,	29

* The recovered starting material (indicated —) was characterised by mixed m. p., specific rotation, and paper chromatography with the lactone spray.[30] The acidic syrups were investigated by paper chromatography, separation on alumina, acetylation, and attempted conversion into the desired 5,6-anhydro-compound by sodium methoxide; no homogeneous compound was obtained.

1,2-O-*Isopropylidene*-5-O-*tosyl*-α-D-*glucofuranurono*-6 ⟶ 3-*lactone*.[5]—Toluene-*p*-sulphonyl chloride (35 g.) in pyridine (75 ml.) was added to 1,2-*O*-isopropylidene-α-D-glucofuranurono-6 ⟶ 3-lactone [24] (33 g.) in pyridine (150 ml.). The mixture was kept at room temperature for 24 hr., then poured on ice, and the resultant crystals were filtered off, washed with water, and dried. Recrystallisation from methanol gave the tosyl-lactone (38 g., 74%), m. p. 185—193°, $[\alpha]_D$ +80° (*c* 1·03 in Me_2CO) (Found: C, 51·5; H, 5·1. Calc. for $C_{14}H_{18}O_8S$: C, 51·9; H, 4·9%).

1,2-O-*Isopropylidene*-5-O-*methanesulphonyl*-α-D-*glucofuranurono*-6 ⟶ 3-*lactone*.—This *lactone* was prepared in the same way as the tosyl derivative, but by using methanesulphonyl chloride (1·1 mol.). It (75%) recrystallised from methanol as needles, m. p. 155—157°, $[\alpha]_D$ +65·5° (*c* 2·02 in Me_2CO) (Found: C, 41·0; H, 5·1. $C_{10}H_{14}O_8S$ requires C, 40·8; H, 4·8%).

Reduction of the Above Lactones.—Attempts to reduce the 5-*O*-tosyl- and 5-*O*-methanesulphonyl-1,2-*O*-isopropylidene-α-D-glucofuranurono-6 ⟶ 3-lactone to the corresponding D-glucofuranose derivatives were made: the details are in Table 2.

Attempted Alkaline Hydrolysis of the Episulphides.—(1) A solution of the L-*ido*-isomer (XII) in 0·1N-methanolic sodium hydroxide was kept at room temperature, and the change of optical rotation observed: $[\alpha]_D$ −15° ⟶ −48° (constant; 24 hr.). When the solution was neutralised with dilute sulphuric acid, the bulk of the reactants separated as a gum which appeared to be polymeric, gave a negative thiol test with sodium nitroprusside, and failed to decolorise iodine solution. Concentration of the mixture under nitrogen, with omission of the neutralisation, failed to yield the sodium salt of the thiol.

[22] Meigh, "Modern Methods of Plant Analysis," Springer Verlag, Berlin, 1955, Vol. II, p. 427.
[23] Haskins, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1946, **68**, 1766.
[24] Owen, Peat, and Jones, *J.*, 1941, 339.
[25] Abdel-Akher, Hamilton, and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 4691.
[26] Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publ. Inc., New York, 1956, p. 510.
[27] Frush and Isbell, *J. Amer. Chem. Soc.*, 1956, **78**, 2844.
[28] Wolfrom and Anno, *J. Amer. Chem. Soc.*, 1952, **74**, 5583.
[29] Glattfeld and Stack, *J. Amer. Chem. Soc.*, 1937, **59**, 753.
[30] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.

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Desulphurisation of the gum with Raney nickel gave a good yield of 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose, m. p. and mixed m. p. 75—77°, and acid-hydrolysis of the latter afforded 5,6-dideoxy-D-*xylo*-hexofuranose (R_G 0·59).

(2) Similar treatment of the D-*gluco*-isomer (XIV) produced a water-insoluble polymer, and a change in optical rotation: $[\alpha]_D$ −73° ⟶ −7° (constant; 24 hr.).

Acid-hydrolysis of the 5,6-*Episulphides.*—5,6-Dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-L-idofuranose (2 g.) was dissolved in dioxan (62·5 ml.) and 2N-sulphuric acid (62·5 ml.), the change in optical rotation being followed polarimetrically at 37°: $[\alpha]_D$ +16·25° (½ hr.), +37·5° (2½ hr.), +36·2° (4½ hr.), 32·2° (6½ hr.), 3·74° (24 hr.). The solution was neutralised with barium carbonate, filtered, and concentrated to a pale-brown syrup which was shown by paper chromatography to contain major components at R_G 0·5 and 0·27, and minor components at R_G 0·15 and 0·11. This syrup was separated on a cellulose column (3·25 × 25 cm.), with butanol half-saturated with water as the mobile phase, into four components: (i) R_G 0·5 (300 mg.), $[\alpha]_D$ +33·3°; (ii) R_G 0·27 (850 mg.), $[\alpha]_D$ −10·8°; (iii) R_G 0·15 (163 mg.); (iv) R_G 0·11 (98 mg.). The total recovery from the column, including the imperfectly separated fractions, was 88%.

Investigation of hydrolysis fraction (i) (R_G 0·5). This syrup reduced Fehling's solution, whereas its precursor did not, and gave a negative thiol test with sodium nitroprusside. Further acid-hydrolysis with 2N-sulphuric acid gave a syrup which showed on a paper chromatogram all four spots of the original hydrolysis mixture. In the same way it was shown that the spot of R_G 0·5 disappeared completely on treatment with 5N-sulphuric acid (24 hr.), to the accompaniment of a large change in specific rotation: $[\alpha]_D$ −6 ⟶ +35°.

A portion of the syrup (38 mg.) was dissolved in dry acetone (100 ml.) containing concentrated sulphuric acid (1 drop), and shaken with anhydrous copper sulphate (2 g.) at room temperature for 48 hr. The mixture was neutralised with ammonia (*d* 0·880), filtered, and concentrated, to give crystals (29 mg.), m. p. 120—135° (sublimes). These recrystallised from chloroform–light petroleum (b. p. 40—60°) and, after vacuum-sublimation, formed needles of 5,6-dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-L-idofuranose (22·4 mg.), m. p. and mixed m. p. 167—169°, the R_G value and infrared spectrum being identical with those of an authentic specimen.

Another portion of this compound (85·8 mg.) in 70% ethanol (20 ml.) was heated under reflux with Raney nickel (*ca.* 2 g.) for 1 hr. The solution was then filtered and concentrated to a syrup (65 mg.), $[\alpha]_D$ 0 ± 3° (*c* 0·72 in H_2O), which did not reduce Fehling's solution and gave a single spot on a paper chromatogram (R_G 0·43) when sprayed with ammoniacal silver nitrate. This value was identical with that of a specimen of 5,6-dideoxy-D-*xylo*-hexitol, prepared by heating 5,6-dideoxy-D-*xylo*-hexofuranose under reflux with Raney nickel.

Periodate Oxidation of 5,6-*Dideoxy*-5,6-*epithio*-1,2-O-*isopropylidenehexoses.*—Aqueous solutions of these compounds (25 mg. in 100 ml.) were oxidised with 0·3M-sodium metaperiodate in unbuffered solution, as described earlier, giving the following results:

		Time (hr.)	2	24	70	94	168
Periodate uptake	L-*ido*-isomer		0·94	1·62	2·62	2·6	2·66
	D-*gluco*-isomer		0·85	1·2	1·5	1·71	2·05

The acid liberated was titrated potentiometrically to pH 6·28 with 0·01N-sodium hydroxide. The L-*ido*-isomer produced 1 mol. (110 hr.); the D-*gluco*-isomer produced 0·5 mol. (110 hr.), rising to 0·7 mol. (160 hr.). After 70 hr. a chromotropic acid determination [31] showed that no formaldehyde was present in either oxidation solution.

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[31] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

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303. *Partial Periodate Oxidation of* D-*Glucitol and its Borate Complex.*

By D. H. Hutson and H. Weigel.

The products of oxidation of D-glucitol with a limited quantity of periodate have been characterised and determined. The results show that the order of susceptibility of the C–C bonds in D-glucitol to cleavage by periodate is: 3,4 (αT-glycol) > 2,3 (αT-glycol) > 4,5 (αC-glycol) > 5,6 (α-glycol) > 1,2 (α-glycol). In borate buffer the favoured complex between D-glucitol and borate involves the participation of the 2- and the 4-hydroxyl group. Under suitable conditions the glucitol–borate complex produces *ca.* 30% of L-xylose.

It has been shown [1] that the oxidation of D-mannitol, galactitol, and D-glucitol with a limited quantity of sodium periodate involves preferential attack on αT-glycol groups (Barker and Bourne's nomenclature [2]). Similar oxidation of erythritol showed that a $CH(OH)\cdot CH_2\cdot OH$ group was more readily cleaved than a $CH(OH)\cdot CH(OH)$ group, but the reverse was found for hexitols.[3] Of acyclic compounds the *threo*- (αT) was oxidised more rapidly than the *erythro*-isomer (αC) and for *threo*-compounds the rate of oxidation decreases with increasing length of the substituents on the glycol group.[4] Thus it became interesting to study quantitatively the relative ease of cleavage of the various C–C bonds of D-glucitol with periodate, particularly as D-glucitol contains two αT- and α-glycol groups, and one αC-glycol group. It was further thought that limited oxidation of D-glucitol in water and in phosphate (pH 10) and borate buffer (pH 10) would clarify the structure of the D-glucitol–borate complex. Buffer of pH 10 was chosen as the concentration of the complexes between polyhydroxy-compounds and borate is greatest in alkali.[5] Characterisation and determination of the products of oxidation were aided by the use of ^{14}C-tracer techniques.

D-Glucitol was separately oxidised in water and in 0·5M-phosphate (pH 10) and 0·5M-borate buffer (pH 10) with 0·25 mol. of sodium periodate. The molar ratio of borate or phosphate to D-glucitol was 3. The products expected from the cleavage of the various C–C bonds were disclosed by chromatographic, ionophoretic, and colorimetric methods. The results shown in Table 1 indicate that 97—100% of the carbon was accounted for.

When oxidised in water, 75% of the D-glucitol remained unchanged and less than 0·1% of the carbon appeared as formic acid (Table 1). As the amount of periodate taken was only 5% of that needed for the complete oxidation of D-glucitol it is likely that the other products arose almost exclusively by direct oxidation of D-glucitol rather than by further oxidation of primary products. It is thus possible to assess the susceptibilities of the various glycol groups of D-glucitol to periodate by calculating the relative amounts of periodate used for the production of the corresponding products.

Table 2 shows that the susceptibilities of the various glycol groups of D-glucitol to periodate fall in the following order: αT > αC > α. Of the two αT- and two α-glycol groups, the 3,4- and the 5,6-group, respectively, are cleaved more readily.

Various mechanisms for the oxidation of glycols by periodate and structures of the intermediate complex, compound or ion, have been suggested. The generally accepted theory [6] is that a cyclic ester intermediate, which may be neutral or mono- or di-negatively

[1] Schwarz, *J.*, 1957, 276.
[2] Barker and Bourne, *J.*, 1952, 905.
[3] Courtois and Guernet, *Bull. Soc. chim. France*, 1957, 1388.
[4] Zuman, Sicher, Kuprička, and Svoboda, *Coll. Czech. Chem. Comm.*, 1958, **23**, 1237.
[5] Foster, *Adv. Carbohydrate Chem.*, 1957, **12**, 81.
[6] Bobbit, *Adv. Carbohydrate Chem.*, 1956, **11**, 1, and references therein.

charged, is formed from the glycol and H_5IO_6 or its dissociation products.* Buist, Bunton, and Miles [7] suggested the formation of an intermediate with a puckered five-atom ring in which the iodine atom is octahedral. They discussed the effect of the stereochemistry and electronic factors of this cyclic intermediate on the equilibrium constant for the formation of the intermediate and the rate constant for the decomposition to products. None of the proposed structures has however been proved. Nor do our results assist towards this or the reaction mechanism; but they are best understood by assuming a planar zig-zag conformation with large substituents in staggered positions,[8] the glycol group being attacked by H_5IO_6 or its dissociation products to form an intermediate with a puckered five-atom ring in which the iodine atom is octahedral.[7]

The O–O distance [9] in crystalline ammonium trihydrogen paraperiodate, $(NH_4)_2H_3IO_6$, in which the iodine is octahedral, is 2·73 Å. This is close to the calculated distance (2·83 Å) for α- and αT-glycol groups in which the large substituents on adjacent carbon atoms are fully staggered.[10] Thus, α- and αT-glycol groups can form with H_5IO_6 cyclic ester intermediates (I and II, respectively) with almost strainless five-atom rings and

TABLE 1. *Oxidation of* D-*glucitol with* 0·25 *mol. of sodium periodate in water and in borate and phosphate buffers* (pH 10).

	In water		In borate		In phosphate	
	Yield		Yield		Yield	
Product	(mol.)	C (%)	(mol.)	C (%)	(mol.)	C (%)
(D-Glucitol)	0·750	75·00	0·912	91·20	0·898	89·80
D-Arabinose	0·005	0·42	0·008	0·66	0·005	0·42
L-Xylose	0·009	0·75	0·021	1·75	0·011	0·92
D-Erythrose	0·047	3·13	0·003	2·00	0·008	0·53
L-Threose	0·015	1·00	0·001	0·07		
DL-Glyceraldehyde	0·269	13·45	0·015	0·75	0·037	1·86
Glycolaldehyde	0·085	2·83	0·072	2·40	0·082	2·73
Formaldehyde	0·015	0·25	0·016	0·27	0·012	0·20
Formic acid	0·005	0·08	0·042	0·70	0·078	1·30
Total		96·91		99·80		97·76

TABLE 2. *Percentage of periodate* (0·25 *mol.*) *consumed by the various* C–C *bonds of* D-*glucitol in water.*

C–C Bond	Type of glycol	Based on yield of:	IO_4^- used (%)	C–C Bond	Type of glycol	Based on yield of:	IO_4^- used (%)
1,2	α	D-Arabinose	2·0	4,5	αC	L-Threose	6·0
5,6	α	L-Xylose	3·6	2,3; 4,5	αT, αC	Glycollaldehyde	34·0
1,2; 5,6	α, α	Formaldehyde	6·0	3,4	αT	Glyceraldehyde	53·8
2,3	αT	D-Erythrose	18·8	Oxidation of products		Formic acid	2·0

without significant distortion of the planar zig-zag conformation of the carbon chain. αC-Glycol groups, the calculated O–O distance [10] of which is 3·68 Å, can form a cyclic intermediate (III) only after considerable distortion of the carbon chain from the planar zig-zag conformation. As the non-bonded interaction in the three cyclic intermediates is (I) < (II) < (III) the order of susceptibility to cleavage by periodate should be α- > αT- > αC-glycol groups.[11] However, α-glycol groups of D-glucitol are least readily attacked by periodate. Whereas the oxygen atoms of αT-glycol groups seem to be already in a position required for the formation of the cyclic ester intermediate, owing to the almost unhindered rotation of the hydroxymethyl groups about the C–C bonds, only a fraction, *f*, of the molecules will have the oxygen atoms of α-glycol groups in this

* [Added 30.11.60.] Since this paper was submitted, Keen and Symons (*Proc. Chem. Soc.*, 1960, 383) have found that ions such as $H_4IO_6^-$ or, possibly, $H_2IO_5^-$ are the major component of saturated aqueous solutions of sodium periodate.

[7] Buist, Bunton, and Miles, *J.*, 1957, 4567; 1959, 743.
[8] McCoubrey and Ubbelohde, *Quart. Rev.*, 1951, **5**, 364.
[9] Helmholtz, *J. Amer. Chem. Soc.*, 1937, **59**, 2036.
[10] Barker, Bourne, and Whiffen, *J.*, 1952, 3865.
[11] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.

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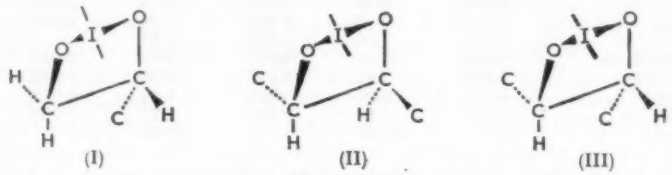
position and an entropy term, $RT \ln 1/f$, has to be added to the free-energy change involved in the reaction. This could make α-glycol groups less susceptible to oxidation by periodate than αT-glycol groups of D-glucitol. For αC-glycol groups, a compression energy term has to be added to the free-energy change of the reaction. It is possible that the difference between these two terms makes the α-glycol groups of D-glucitol least readily attacked by periodate.

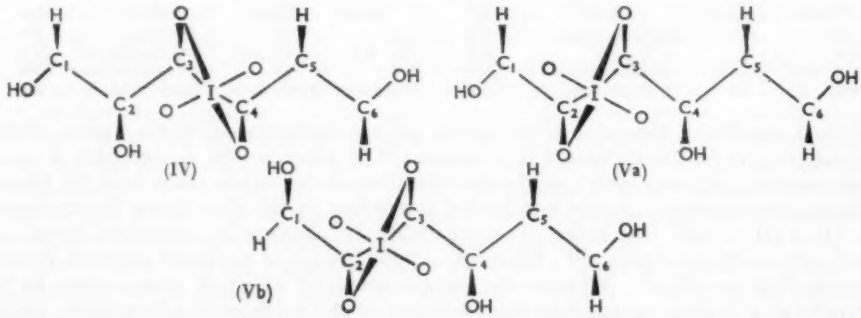
The difference in ease of cleavage of the two αT-glycol groups can be due to the stereochemistry of the ester intermediates. In (IV) and (V) the hypothetical intermediates involving $C_{(3)}$–$C_{(4)}$ and $C_{(2)}$–$C_{(3)}$, respectively, are depicted with a puckered five-atom ring in which the iodine atom is octahedral. In (IV) and (Va) the 1- and 6-hydroxyl groups extend the planar zig-zag conformation of the carbon chain: in both cases a hydroxyl group and a hydrogen atom, $HO_{(2)}$, and $H_{(5)}$, $HO_{(4)}$ and $H_{(1)}$, respectively, lie close to two of the oxygen atoms attached to the iodine atom. The situation remains the same when the hydroxymethyl groups of (IV) rotate freely. However, a fraction of the molecules of (V) will have the 1-hydroxyl group in a position as shown in (Vb), in which two hydroxyl groups, $HO_{(1)}$ and $HO_{(4)}$, lie close to two of the oxygen atoms attached to the iodine atom. The resulting greater steric compression could make the αT-glycol group involving $C_{(2)}$ and $C_{(3)}$ less susceptible to oxidation by periodate than that involving $C_{(3)}$ and $C_{(4)}$.

Since it is established that αT-glycol groups are more readily oxidised by periodate than αC-glycol groups it is reasonable to assume that, in a statistical sense, the 5-hydroxyl group is more readily available for the formation of an intermediate involving $C_{(5)}$ and



(I) (II) (III)

Four of the oxygen atoms attached to the iodine atom are omitted. Two of these lie towards the observer in positions equivalent to the oxygen atoms attached also to the carbon atoms.



(IV) (Va) (Vb)

Atoms lying below the plane of the carbon atoms and two of the oxygen atoms attached to the iodine atom are omitted. The latter lie towards the observer in positions equivalent to O_3, O_4 and O_3, O_3, respectively.

$C_{(6)}$ than the 2-hydroxyl group for the formation of an intermediate involving $C_{(1)}$ and $C_{(2)}$. Thus, of the two α-glycol groups, the 5,6-bond is more readily cleaved than the 1,2-bond.

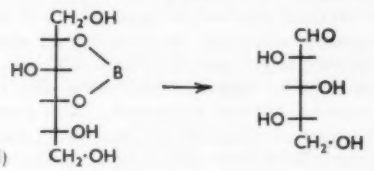
It was now possible to examine the effect of borate ions on the reaction. From the sequence of M_G values of substituted aldoses in borate solution at pH 10, Foster [5] concluded that the *aldehydo*-form of D-glucose is the principal one involved in complex formation

and the pair of the 2- and the 4-hydroxyl group are sterically most favourable for complex formation. This, and the relative stabilities of cyclic acetals of D-glucitol,[10] suggested that a similar complex is favoured for D-glucitol. Partial periodate oxidation of such a complex (VI) should yield a larger quantity of L-xylose (VII) than a reaction in the absence of borate.

There was a possibility of anomalous reactions at pH 10.[7] Certain discrepancies have been found in the periodate oxidation in phosphate buffer at pH 7·5.[12] It was thought that similar discrepancies might arise with a borate buffer and that comparison between the oxidation of D-glucitol in 0·5M-borate (pH 10) and 0·5M-phosphate buffer (pH 10) would be valid.

Oxidation of D-glucitol with 0·25 mol. of sodium periodate in the presence of borate (pH 10) or phosphate (pH 10) yielded very different results from those obtained with the unbuffered solution (Table 1). Only *ca.* 10% of the D-glucitol was oxidised in the alkaline solutions whereas the theoretical amount of 25% was oxidised in the unbuffered solution. Extensive secondary reactions (cf. formic acid production) under the alkaline conditions made detailed comparison with the unbuffered solution impossible.

The ratios of the yields of L-xylose to D-arabinose (primary reactions) in the unbuffered, borate-, and phosphate-buffered solutions are 1·8, 2·6, and 2·2, respectively. The ratios of the yield of L-xylose in borate- and phosphate-buffered solutions relative to that in the unbuffered solution are 2·3 and 1·2, respectively. This indicated that the yield of L-xylose could be significantly increased by the presence of borate ions. Accordingly, D-glucitol dissolved in 4M-borate buffer (pH 10·7) (borate to D-glucitol ratio 5 : 1) was oxidised with 2·5 mol. of sodium periodate. The component which had been characterised by carrier



(VI) (VII)

dilution analysis as L-xylose was the major product. This was separated by paper chromatography and determined quantitatively. It was found that the yield of L-xylose could be raised in this way to *ca.* 30%.

The results indicate that D-glucitol forms a complex with borate ions similar to that of D-glucose,[5] *i.e.*, participation of $HO_{(2)}$ and $HO_{(3)}$. However, a complex involving $HO_{(1)}$ and $HO_{(4)}$ is not excluded as the resulting 7-atom ring could have the 2- and the 3-hydroxyl group in *trans*-relation, when they would react with periodate more slowly than a $CH(OH)\cdot CH_2\cdot OH$ group.[13] On the other hand, it has been shown [14] that borate ions have no tendency to form complexes involving 7-atom or larger rings. The results clearly establish that the principal site of attack of periodate on the D-glucitol–borate complex is the 5,6-bond. The pair of hydroxyl groups involved in the formation of the complex are probably those on $C_{(2)}$ and $C_{(4)}$.

It is of interest that complex-formation with boric acid has been used similarly to effect selective substitution in D-glucose,[15,16] D-mannitol,[15,17] D-glucose diethyl mercaptal,[15] and methyl α- and β-glucopyranoside,[18] and to block the oxidation of carbohydrates in tissues by lead tetra-acetate.[19]

[12] Bell, Palmer, and Johns, *J.*, 1949, 1536; Bell and Greville, *J.*, 1950, 1902.
[13] Bourne, Hartigan, and Weigel, *J.*, 1961, 1088.
[14] Frahn and Mills, *Chem. and Ind.*, 1956, 578.
[15] Brigl and Grün, *Annalen*, 1932, **495**, 60.
[16] von Vargha, *Ber.*, 1933, **66**, 704.
[17] von Vargha, *Ber.*, 1933, **66**, 1394.
[18] Bell, *J.*, 1935, 175; Sugihari and Peterson, *J. Amer. Chem. Soc.*, 1956, **78**, 1760.
[19] Staple, *Nature*, 1955, **176**, 1125; *J. Histochem. Cytochem.*, 1957, **5**, 472.

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Experimental

Materials.—D-[^{14}C]Glucitol, uniformly labelled, was obtained from the Radiochemical Centre, Amersham. Glycollaldehyde was prepared as described by Powers *et al.*[20]

Chromatography.—The solvents used in chromatography were (*a*) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 2); (*b*) ethyl acetate–acetic acid–water (9 : 2 : 2); (*c*) methyl ethyl ketone saturated with water; [1] (*d*) butan-1-ol–ethanol–water (4 : 1 : 5) (organic phase).

Determination of Radioactivity.—Radioactivities were determined after conversion of the compound into carbon dioxide, and thence into barium carbonate.[21] The amount used was sufficient to give a thickness of greater than 20 mg. per cm.^{2}. The β-emission of a radioactive specimen was measured by means of a Geiger–Müller end-window counter and for times sufficient to give a standard counting error of less than ±2%.

Periodate Oxidations.—To mixtures of 0·166M-aqueous D-glucitol (1 mol.) with 0·5M-borate buffer (pH 10·6; 3 mol.) or 0·5M-phosphate buffer (pH 10·1; 3 mol.) (final pH 10·0) was added standard sodium periodate solution (0·25 mol.). After 10 min., Amberlite IR-120(H$^+$) was stirred into the buffered solutions to adjust the pH to 5.

Identification of Products.—D-Glucitol, D-arabinose, L-xylose, and DL-glyceraldehyde were identified by paper chromatography in solvents (*a*) and (*b*) and by treatment of the chromatograms with acetone–silver nitrate–alcoholic sodium hydroxide [22] or *p*-anisidine hydrochloride in butanol.[23] D-Erythrose and L-threose were separated from other products by paper chromatography in solvent (*c*),[1] resolved, and identified by paper ionophoresis in molybdate solution.[24] Glycollaldehyde was shown to be present by treatment with diphenylamine in acetic acid and measurement of absorption at 680 mμ.[25] Formaldehyde was shown to be present by the chromotropic acid method.[26] Formic acid was assumed to constitute the total titratable acid present.

Characterisation and Determination of Products.—(i) *D-Glucitol, D-arabinose, and L-xylose.* D-[^{14}C]Glucitol was separately oxidised with sodium periodate (0·25 mol.) in water, 0·5M-borate buffer (pH 10), and 0·5M-phosphate buffer (pH 10) as described above. A carrier compound (D-glucitol, D-arabinose, or L-xylose) was dissolved in each solution and allowed to equilibrate overnight. Boric acid was removed by repeated distillation with methanol, and phosphoric acid by precipitation with aqueous barium hydroxide. The products were separated by chromatography on Whatman paper no. 3 in solvent (*a*). D-[^{14}C]Glucitol was converted into the hexa-acetate which was recrystallised from ethanol until consecutive samples possessed constant m. p. and specific radioactivity. D-Arabinose and L-xylose were converted into their phenylosazones which were recrystallised twice from water and twice from benzene, after which consecutive samples possessed constant m. p. and specific radioactivity. The details of the analysis are shown in Table 3.

(ii) *D-Erythrose and DL-glyceraldehyde.* D-[^{14}C]Glucitol samples were oxidised with sodium periodate (0·25 mol.) as described above. The solutions were treated with potassium borohydride at room temperature for 12 hr. and then with Amberlite IR-120(H$^+$). Erythritol and glycerol were added as carrier compounds. After equilibration for 1 hr. boric acid was removed by repeated distillation with methanol. [^{14}C]Erythritol and [^{14}C]glycerol were separated by chromatography on Whatman paper no. 3 in solvent (*d*) and converted into the tetra- and tri-benzoate, respectively, which were recrystallised from aqueous pyridine and aqueous ethanol, respectively, until consecutive samples possessed constant m. p. and specific radioactivity. The details of the analysis are shown in Table 3.

(iii) *L-Threose.* D-[^{14}C]Glucitol (20 mg.) was separately oxidised with sodium periodate (0·25 mol.) in water and 0·5M-borate buffer (pH 10) as described above. The borate-buffered solution was treated with Amberlite IR-120(H$^+$), and the boric acid removed as above. L-[^{14}C]Threose and D-[^{14}C]erythrose were separated by paper chromatography in solvent (*c*).

[20] Powers, Tabakoglu, and Sable, *Biochem. Prep.*, 1955, **4**, 56.
[21] Skipper, Bryan, White, and Hutchison, *J. Biol. Chem.*, 1948, **73**, 371; Calvin, Heidelberger, Reid, Tolbert, and Yankwich, "Isotopic Carbon," Wiley, New York, 1949; Henriques, Kistiakowsky, Margnetti, and Schneider, *Ind. Eng. Chem. Analyt.*, 1946, **18**, 349.
[22] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[23] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[24] Bourne, Hutson, and Weigel, *Chem. and Ind.*, 1959, 1047.
[25] Dische and Borenfreund, *J. Biol. Chem.*, 1949, **180**, 1297.
[26] Adcock, *Analyst*, 1957, **82**, 427.

The eluted tetroses were subjected to ionophoresis in molybdate solution (pH 5).[24] *p*-Anisidine hydrochloride in butanol and ultraviolet light [23] revealed the positions of the tetroses on the ionophoretograms. From a comparison of the β-emission of the two spots the ratio of the yields of L-threose and D-erythrose was found. The yield of L-threose was calculated from the results of the determination of D-erythrose. The results are shown in Table 4.

TABLE 3. *Carrier dilution analysis of products from oxidation of* D-[^{14}C]*glucitol with* 0·25 *mol. of sodium periodate.*

W_G (mg.)	S_o (μc per g.-atom of carbon)	Product	Medium	W_c (mg.)	M. p. of deriv.	S_i (μc per g.-atom of carbon)	Yield (mol.)
72	3164	(D-Glucitol)	Water	250	99°	561·90	0·750
72	3164	D-Arabinose	Water	254	163	3·43	0·005
72	3164	L-Xylose	Water	341·4	164	5·03	0·009
72	3164	D-Erythrose *	Water	242·3	185	29·40	0·047
72	3164	DL-Glyceraldehyde †	Water	254	72	117·52	0·269
72	3164	(D-Glucitol)	Borate	247	99	664·40	0·912
72	3164	D-Arabinose	Borate	233	163	6·14	0·008
72	3164	L-Xylose	Borate	226	164	17·54	0·021
72	3164	D-Erythrose *	Borate	256	185	1·77	0·003
72	3164	DL-Glyceraldehyde †	Borate	242·3	72	7·06	0·015
400	821	(D-Glucitol)	Phosphate	724·7	98	272·00	0·898
72	3164	D-Arabinose	Phosphate	275·1	163	3·24	0·005
72	3164	L-Xylose	Phosphate	195·5	164	10·25	0·011
72	3164	D-Erythrose *	Phosphate	255·3	185	4·71	0·008
72	3164	DL-Glyceraldehyde †	Phosphate	242·3	72	17·66	0·037

W_G = Weight of D-[^{14}C]glucitol oxidised. S_o = spec. radioactivity of D-[^{14}C]glucitol. W_c = weight of carrier added. S_i = spec. radioactivity of parent compound of isolated derivative.
* Carrier compound was erythritol. † Carrier compound was glycerol.

TABLE 4. *Determination of* L-*threose from oxidation of* D-[^{14}C]*glucitol with* 0·25 *mol. of periodate.*

Product	Medium	Radioactivity (counts per min.)	Ratio, L-threose : D-erythrose	Yield of L-threose * (mol.)
L-Threose	Water	216	0·31	0·015
D-Erythrose	Water	693		
L-Threose	Borate (pH 10)	50	0·23	0·001
D-Erythrose	Borate (pH 10)	222		

* Based on yield of D-erythrose.

(iv) *Glycollaldehyde.* The results of Dische and Borenfreund [25] show that glycollaldehyde, after treatment with diphenylamine in acetic acid, can be determined by measurement of the optical density at 680 mμ and that the presence of glyceraldehyde will cause an error not greater than *ca.* 3%. Measurement of the optical density of standard solutions of glycollaldehyde (0·1%) containing also D-erythrose, formate, phosphate, borate, and iodate showed that only the latter interfered seriously with the determination of glycollaldehyde. Iodate was thus removed from the unbuffered and phosphate-buffered reaction mixtures by treatment with Amberlite IRA-400(OAc). To avoid possible loss of glycollaldehyde by adsorption on the resin as the glycollaldehyde–borate complex, the borate-buffered reaction mixture was treated with much glucitol, with which borate reacts preferentially, before treatment with the resin.

D-Glucitol (0·91 g.) was oxidised as described above. After removal of the iodate, glycollaldehyde was determined colorimetrically.[25] The measurement of the optical densities at 680 mμ (Ilford filter no. 608) of the solutions obtained from the unbuffered and borate- and phosphate-buffered mixtures corresponded to yields of 0·085, 0·072, and 0·082 mole of glycollaldehyde per mole of D-glucitol, respectively.

(v) *Formaldehyde.* D-Glucitol (0·91 g.) was oxidised as described above. After removal by steam-distillation from the reaction mixtures, formaldehyde was determined by the chromotropic acid method.[26] Measurement of the optical densities (Ilford filter no. 606) of the solutions obtained from the unbuffered and borate- and phosphate-buffered mixtures corresponded to yields of 0·015, 0·016, and 0·012 mole respectively of formaldehyde per mole of D-glucitol.

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(vi) *Formic acid.* D-Glucitol (0·91 g.) was separately oxidised as described above. Formic acid was determined by titration with 0·01N-sodium hydroxide, a pH-meter being used for end-point detection. A blank titre was found after oxidation of ethylene glycol with 0·125 mol. of sodium periodate. From the buffered solutions the formic acid was first separated by acidification and distillation of the reaction mixture. True titres: 2·5 ml. (water), 21·0 ml. (borate buffer), 39·0 ml. (phosphate buffer). These correspond to yields of 0·005, 0·042, and 0·078 mole, respectively, of formic acid per mole of D-glucitol.

Determination of L-*Xylose from Oxidation of* D-*Glucitol in* 4M-*Borate Buffer* (5 *Mol.*) *with* 2·5 *Mol. of Sodium Periodate.*—To a solution of D-glucitol (1·82 g.) in 4M-borate buffer (pH 10·7) (12·5 ml.) was added a solution of sodium periodate (5·45 g.) in water (25 ml.). After 10 min. sodium ions and boric acid were removed by treatment with Amberlite IR-120(H^+) and repeated distillation with methanol, respectively. The residue was extracted with methanol. Paper chromatography in solvent (*a*) showed that the major component had an R_F value identical with that which had been characterised by carrier dilution analysis as L-xylose. Elution and quantitative determination of this component by the anthrone method [27] showed a 30·6% yield.

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[27] Bailey, *Biochem. J.*, 1958, **68**, 669.

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304. *The Vibrational Spectra and Structures of Dithionate, Hypophosphate, and Related Ions.*

By W. G. PALMER.

Complete assignment of the vibrational frequencies observed in the spectra of dithionate and hypophosphate reveals the close structural similarity of these ions and appears to demand the symmetry D_{3d} for hypophosphate as well as for dithionate. The spectra of the acid ion $H_2P_2O_6^{2-}$ and of diphosphate $P_2O_7^{4-}$ are compared with those of hypophosphate. The relation of vibrational frequencies to bond strengths and orders in the oxy-anions of sulphur and phosphorus is briefly discussed.

ALTHOUGH the formula $H_4P_2O_6$ has long been accepted for hypophosphoric acid, there is still some doubt about the structure of the corresponding ion $P_2O_6^{4-}$. No examination by *X*-ray diffraction leading to definite atomic positions in a hypophosphate has yet appeared, although a preliminary study of the salt $(NH_4)_2H_2P_2O_6$ resulted in tentative suggestions about the structure of the ion $H_2P_2O_6^{2-}$.[1] Raman spectra of aqueous solutions of the pure acid and of the salts $K_2H_2P_2O_6$ and $(NH_4)H_3P_2O_6$ have been observed but the polarization properties were not recorded.[2,3] It has been proved [4,5] that on controlled oxidation of hypophosphate by halogens the sole product is diphosphate. Although it is possible to explain this observation on the basis of structure (II),[5] yet structure (I) seems the more natural deduction for the hypophosphate ion. On the other hand, examination of hypophosphate by the method of nuclear magnetic resonance has strongly supported the symmetrical formula (II).[6]

[1] Raistrick and Hobbs, *Nature*, 1949, **164**, 113.
[2] Gupta and Majumdar, *J. Indian Chem. Soc.*, 1942, **19**, 286.
[3] Baudler, *Z. anorg. Chem.*, 1955, **279**, 115.
[4] Blaser and Halpern, *Z. anorg. Chem.*, 1933, **215**, 33; Blaser, *Chem. Ber.*, 1953, **86**, 563.
[5] Palmer, *J.*, 1961, 1079.
[6] Callis, Van Wazer, Schoolery, and Anderson, *J. Amer. Chem. Soc.*, 1957, **79**, 2719.

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It is plain that structure (I) or (II) could be excluded if both the infrared and Raman spectra of the ion were adequately known. The structures correspond to two extreme relations between the two types of spectra: all fundamentals of (I) will in principle be active in both spectra, while the two spectra of (II), if as is most probable it has the

symmetry D_{3d}, will contain no frequencies in common (Table 1). Further evidence can be sought in the relations between the spectra of $P_2O_6^{4-}$ and $S_2O_6^{2-}$, which has been conclusively assigned the structure analogous to (II) by *X*-ray methods.[7] Although the experimental difficulty of observing a complete Raman spectrum of $P_2O_6^{4-}$ frustrated this simple and direct approach, it can at least be claimed that the present investigation has produced no support for (I) and much evidence in favour of (II).

In general, the observation and analysis of the infrared and Raman spectra of a compound afford a means of discovering its structure ranking in power with diffraction methods (if the structure has a fair degree of symmetry), but some disturbing features enter when the compound is an oxy-anion. It is then probably impossible to observe spectra of which the frequencies are entirely specific to the ion, and owe nothing to its environment, which may include the chemical nature, size, and charge of the cation, and the presence of water of hydration when observations are made upon crystal powders or " mulls; " nor can the effect of an environment of water in the concentrated solutions employed for the Raman effect be excluded. Such influences upon frequencies appear to be sporadic and usually vary both in sign and magnitude over the range of frequencies concerned, so that corrections for shift, from one salt to another, from solution to crystal, or even from a Nujol mull preparation to that of a KBr disc, are valid over only short ranges.

It appears wise to rely, for structural purposes, mainly on salts of the alkali metals, and to employ them, when normally hydrated, in anhydrous condition whenever the removal of water of hydration can be isolated from further possible decomposition. In spite, however, of such obvious precautions, it is not to be expected that absolute frequencies can be assigned to fundamentals and combination bands of such ions as are concerned in the present investigation with the precision attainable in the study of volatile, electrically neutral compounds. For such reasons correlation with the behaviour of a neutral compound of parallel type and comparable force constants, such as C_2F_6, the spectra of which have been fully analysed,[8] has proved helpful during the present work.

Of the 18 possible fundamentals of a molecule or ion A_2X_6 of symmetry D_{3d}, eight of type *u* and nine of type *g* are allowed only in the infrared and Raman spectra respectively (Table 1). In each set of fundamentals, six, being doubly degenerate (E_u and E_g) yield only three frequencies. Therefore, if $P_2O_6^{4-}$ has structure (II) with symmetry D_{3d} a full assignment of its spectra must show in all 11 distinct frequencies, five in the infrared and six in the Raman spectrum. It is to be expected that the highest four frequencies [one doubly degenerate (*E*) and one single (*A*) in each spectrum] will correspond to P–$(O)_3$ stretching vibrations, followed at a much lower average frequency by the four P–$(O)_3$ deformation frequencies (also one doubly degenerate and one single in each spectrum). Lastly, at the lowest frequencies will come the vibrations in which PO_3 acts principally as a single, heavy unit: PO_3–PO_3 stretching and rocking. For ions related in structure to $P_2O_6^{4-}$, such as the acid ion $H_2P_2O_6^{2-}$, diphosphate $P_2O_7^{4-}$, and phosphite HPO_3^{2-}, the lower symmetry permits all (or nearly all) of the vibrations to be active in the infrared spectrum, which for all these ions is more readily accessible than the Raman spectrum.

[7] Barnes and Wendling, *Z. Krist.*, 1938, **99**, 153; Stanley, *Acta Cryst.*, 1953, **6**, 187; Martinez, Garcia-Blanco, and Rivoir, *ibid.*, 1956, **9**, 145.

[8] Nielson, Richards, and McMurry, *J. Chem. Phys.*, 1948, **16**, 67; Nielson and Gullikson, *ibid.*, 1953, **21**, 1416.

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In the task of assigning frequencies to $P_2O_6^{4-}$ it is therefore very helpful to consider related frequencies in the infrared spectra of these other ions.

Experimental

Infrared spectra were observed on a Perkin–Elmer spectrophotometer No. 21, in the range 5000—400 cm.$^{-1}$ (2—25 μ, NaCl and KBr prisms) for alkali-metal dithionates and hypophosphates, and in the NaCl range (5000—625 cm.$^{-1}$) for the latter salts of a number of other cations. As far as possible, hydrated salts were rendered anhydrous before being " mulled " in Nujol or hexachlorobutadiene, or distributed in a KBr disc. An infrared spectrum in the NaCl range for a saturated solution of $K_4P_2O_6$ was successfully obtained from a film between silver chloride plates. The Raman spectrum of the same concentrated solution was examined in the Laboratory of Inorganic Chemistry at Oxford by the most generous co-operation of Dr. L. A. Woodward, who reported that the ion $P_2O_6^{4-}$, like the corresponding di-acid ion,[3] proved to be an intrinsically weak scatterer, and only three frequencies (out of a possible six for symmetry D_{3d}) could be identified. Fortunately, the well-defined combination frequencies observable in the infrared spectra allowed the remaining Raman frequencies to be calculated satisfactorily, and those observed to be confirmed.

Raman spectra of sodium dithionate have been fully explored for aqueous solution,[9] and sufficiently for the crystalline powder,[10] to ascertain the shift in frequencies on passing from the dissolved to the crystalline state. The infrared spectra of sodium and potassium dithionates have been re-examined, as doubt existed about the absolute frequencies previously published.[11]

Preparation and Purity of Materials.—(a) *Dithionates.* The sodium salt $Na_2S_2O_6,2H_2O$ and the anhydrous potassium salt were obtained by oxidation of sulphite with silver nitrate.[12] When finally purified neither of the salts gave any qualitative indication for nitrate or sulphate, nor did the infrared spectra reveal any known frequency of these ions. At 115° *in vacuo* the sodium salt lost 14·88% as water, and the resulting solid 31·2% as SO_2 on ignition (Calc.: 14·87 and 31·1%, respectively). The potassium salt lost 27·0% as SO_2 on ignition (Calc.: 27·0%).

(b) *Hypophosphates.* The salts required were obtained by standard operations from an initial stock of sodium hypophosphate prepared as described elsewhere,[5] where will also be found the methods by which purity was confirmed. Particular care was taken to ascertain that salts requiring dehydration suffered thereby no chemical change other than loss of water. To observe the Raman spectrum of $P_2O_6^{4-}$ three nearly saturated aqueous solutions of $K_4P_2O_6$ were prepared from pure $K_2H_2P_2O_6,2H_2O$ and potassium hydroxide, containing respectively 10, 25, and 50% excess of potassium hydroxide over that required stoicheiometrically. All three solutions gave identical spectra.

Results and Discussion

The terminology to be used is set out in Table 1.

Dithionate, $S_2O_6^{2-}$.—For dithionate ion it has been possible to assign all eleven frequencies allowed for the symmetry D_{3d} and to amplify the *X*-ray analysis. The fundamentals listed in Table 9 are referable to the anhydrous sodium salt, although for $S_2O_6^{2-}$ the frequency shifts between the anhydrous sodium and potassium salts, and between preparations of the sodium salt under various conditions, are slight and no corrections were attempted. In assigning the combination frequencies (Table 2), which for symmetry D_{3d} follow the $g \times u$ rule, fundamentals, with the exception of ν_{12}, have been taken from observations on the powdered dihydrate, $Na_2S_2O_6,2H_2O$. Assignments of the six Raman frequencies, which fall into the expected three pairs, follow almost automatically from their polarization properties. The totally symmetrical breathing frequency ν_1 is, as in most other cases, by far the most intense in the Raman spectrum, especially when observed in aqueous solution, and as usual the degenerate frequencies E_g are all notably weaker than their non-degenerate counterparts A_{1g}.

[9] Gerding and Eriks, *Rec. Trav. chim.*, 1950, **69**, 724.
[10] Eucken and Wagner, *Acta Phys. Austrica*, 1947—48, **1**, 339.
[11] Lecomte and Duval, *Compt. rend.*, 1943, **217**, 42; *Bull. Soc. chim. France*, 1944, **11**, 376.
[12] Baubigny, *Ann. Chim. Phys.*, 1910, **20**, 5; Palmer, " Experimental Inorganic Chemistry," Cambridge, 1954, p. 361.

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TABLE 1. *Classification of infrared and Raman fundamental frequencies.*

	Type of vibation	Infrared spectrum		Raman spectrum	
A_2X_6: D_{3d}	A–X stretching	ν_5, A_{2u}	ν_7, E_u	ν_1, A_{1g}	ν_{10}, E_g
	AX_3 deformation	ν_6, A_{2u}	ν_8, E_u	ν_2, A_{1g}	ν_{11}, E_g
	A–A stretching			ν_3, A_{1g}	
	AX_3 rocking		ν_9, E_u		ν_{12}, E_g
	AX_3–AX_3 torsion	ν_4, A_{1u} *			

* Inactive as a fundamental.

A_2X_6: D_{3h} Frequencies as for D_{3d}, with the addition that ν_7, ν_8, and ν_9 may also occur in the Raman spectrum (as depolarized radiation).

Vibrations of species A_{1g} give polarized radiation, and those of species E_g depolarized radiation, in the Raman spectrum.

HAX_3: C_{3v}	Infrared and Raman spectra	
(HA)–X stretching	ν_2, A_1	ν_5, E
$(HA)X_3$ deformation	ν_3, A_1	ν_6, E

(The numbering of the fundamentals follows that of Herzberg, "Infrared and Raman Spectra of Polyatomic Molecules," New York, 1946.)

TABLE 2.*

Dithionates — *Observed frequencies* ($cm.^{-1}$)

Infrared spectra (preparation in Nujol mull unless otherwise stated).

$Na_2S_2O_6,2H_2O$	$Na_2S_2O_6$	$K_2S_2O_6$	Assignment
2320 (w)	2326 (w)	2326 (m)	$\nu_1 + \nu_7$ (2337)
2198 (m)	2203 (s)	2208 (s)	$\nu_{10} + \nu_5$ (2216)
2083 (s)	2088 (m)	2083 (m)	$\nu_1 + \nu_5$ (2102)
1240 (10, v sp)	1235 (10, v sp)	1240 (10, v sp) 1212 (4, v sp)	ν_7, E_u
1000 (9, v sp)	1000 (9, v sp)	996 (7, v sp)	ν_5, A_{2u}
760 (s)	760—700 (sh)	760—770 (sh) 707 (s) [1], 710 (m) [2], 711 (w) [3]	$\nu_{11} + \nu_9$ $\nu_5 - \nu_3$ (707)
N.I.	N.I.	584 (10, v sp) [1] 570 (10, v sp)	ν_6, A_{2u}
N.I.	N.I.	514 (5, v sp) [1] 518 (8, v sp)	ν_8, E_u

Raman spectra

$Na_2S_2O_6$ (aqueous solution)	$Na_2S_2O_6,2H_2O$ (crystal powder)	Assignment
1206 (1, dp)	1216 (4, dp)	ν_{10}, E_g
1092 (10, p)	1102 (7, p)	ν_1, A_{1g}
710 (6, p)	710 (6, p)	ν_2, A_{1g}
550 (1, ?)	556 (0, dp ?)	ν_{11}, E_g
320 (4, ?)	—	ν_{12}, E_g
281 (8, p)	293 (4, p)	ν_3, A_{1g}

* Maximum of intensity scale for fundamentals, 10: v sp, very sharp. Intensities of combination frequencies: s, strong; m, medium; w, weak; sh, shoulder.

[1] Preparation in KBr disc: spectrum in KBr range. [2] Preparation in hexachlorobutadiene mull: spectrum in KBr range. [3] Preparation in Nujol mull: spectrum in NaCl range: combination frequency completely resolved from Nujol frequency at 720 $cm.^{-1}$.

Raman spectra: p, polarized; dp, depolarized. N.I.: Not investigated.

In the infrared spectrum of sodium dithionate and its dihydrate two sharply defined fundamentals are observed in the NaCl range, and the higher of these is sharply resolved into a doublet in the corresponding spectrum of potassium dithionate. Such splitting is taken to mean that the frequency is that of a degenerate vibrational mode and may be assigned as ν_7, E_u, leaving the lower frequency, at about 1000 $cm.^{-1}$, as ν_5, A_{2u}. The corresponding fundamental ν_7 from the hydrated sodium salt is not resolved but definitely shows indications of a shoulder. Both the potassium and the hydrated sodium salt have 4 molecules per unit cell, with complicated but quite different crystal structures from which a specific cause of the removal of degeneracy is not easily discerned. Although neither of the very sharply defined fundamentals round 577 and 516 $cm.^{-1}$ in the spectrum

of potassium dithionate in the KBr range reveals degeneracy in a similar way, they are assigned respectively to the deformation frequencies ν_6, A_{2u} and ν_8, E_u by analogy with corresponding frequencies in hypophosphate spectra, where, as will appear later, the reasons for the particular assignment are rather clearer.

The three high combination frequencies, well defined in all the spectra observed, are easily and unambiguously assigned as shown in Table 2. If the two lower frequencies at 760 and 710 cm.$^{-1}$ are both regarded as binary summation terms their possible Raman constituents are ν_3, ν_{11}, and ν_{12}. Since there are certainly no infrared-active fundamentals in the observed range from near the lower limit of the KBr range at 400 cm.$^{-1}$ to ν_8 at 518 cm.$^{-1}$, we derive the possible frequencies 154, 204, and 390 cm.$^{-1}$ from which to select the two remaining fundamentals ν_9 (symmetrical SO_3 rocking) and ν_4 (torsion round the S–S axis). The frequency ν_9 will very probably be lower than that of the unsymmetrical rocking ν_{12} observed in the Raman spectrum at 320 cm.$^{-1}$; moreover the assignment of ν_9 as 204 cm.$^{-1}$ falls appropriately into the group of degenerate frequencies E_u:

E_u	C_2F_6	$S_2O_6^{2-}$
ν_7	1251	1240
ν_8	523	518
ν_9	216	204

As ν_4 will certainly enter as the minimal fundamental, we could select for this 154 cm.$^{-1}$, and assign the frequency at 710 cm.$^{-1}$ as ν_{11}, $E_g + \nu_4$, A_{1u}, a combination allowed in both symmetries D_{3d} and D_{3h}. However, it is equally possible to assign this frequency as the *difference* term $\nu_5 - \nu_3$, as shown in Table 2. In spite of careful search,[8] no combination frequency involving ν_4 could be traced in the whole extent of the infrared spectrum of C_2F_6, nor do any such occur with certainty in the spectrum of C_2H_6. Since the term $\nu_5 - \nu_3$ does occur unambiguously (though weakly) in the C_2F_6 spectrum, it may be presumed to represent the most probable interpretation of the $S_2O_6^{2-}$ frequency at 710 cm.$^{-1}$. The corresponding summation term would be masked by its proximity to the very intense fundamental ν_7.

The coincidence of the infrared frequency round 710 cm.$^{-1}$ with the Raman frequency assigned as ν_2 is certainly fortuitous. In the three separately observed infrared spectra in which fundamentals as well as the frequency 710 cm.$^{-1}$ occur, the last, although always very sharply defined, has only the secondary intensity appropriate to a combination frequency. If $S_2O_6^{2-}$ possessed the ("eclipsed") symmetry D_{3h} then the fundamentals ν_7, ν_8, and ν_9 could appear in both the infrared and the Raman spectra, but in all three cases as depolarized radiation in the latter. On the contrary, the radiation of the frequency ν_9, which shows high intensity in both Raman spectra, is quite certainly polarized.

Diphosphate, $P_2O_7^{4-}$.—From a Nujol mull of the anhydrous sodium salt, obtained from the pure decahydrate by heating it *in vacuo* at 115°, the following fundamentals were observed in the NaCl range of the infrared spectrum:[13]

cm.$^{-1}$		cm.$^{-1}$
1152 (10) }	partially resolved, sp	987 (5, v sp)
1121 (10) }		917 (10, m)
1030 (5, v sp)		735 (10, v sp)

(Maximum of intensity scale, 10: v sp, very sharp; sp, sharp; m, medium definition.)

The ion $P_2O_7^{4-}$ has symmetry C_{2v}[14] and none of the possible stretching vibrations of the PO_3 groups is degenerate. Consequently, six distinct frequencies are to be expected ($2A_1$, $2B_1$, A_2, and B_2) of which only one, A_2, is forbidden in the infrared spectrum. It seems clear that at least four of the remaining five frequencies are included in the infrared range 987—1152 cm.$^{-1}$. The frequencies at 917 and 735 cm.$^{-1}$ may plausibly be assigned to two of the three possible P–O–P vibrations, all of which are active in the infrared region.

[13] Cf. Corbridge and Lowe, *J.*, 1954, **493**.
[14] MacArthur and Beevers, *Acta Cryst.*, 1957, **10**, 428.

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Hypophosphate Ions.—(1) *The di-acid ion* $H_2P_2O_6^{2-}$. It must be assumed in view of the dissociation constants of hypophosphoric acid [15] that the Raman spectra of concentrated solutions of the free acid and of the salts $(NH_4)H_3P_2O_6$ and $K_2H_2P_2O_6$ previously observed [2,3] relate to the ion $H_2P_2O_6$ and not to $P_2O_6^{4-}$. The relation of the infrared spectrum of $Na_2H_2P_2O_6$ to these Raman spectra fully bears out this assumption (Table 3).

TABLE 3.* *Sodium dihydrogen hypophosphate,* $Na_2H_2P_2O_6$.

Infrared (cm.$^{-1}$) $Na_2H_2P_2O_6$ (nm.) (NaCl and KBr ranges)	Raman * (cm.$^{-1}$) $(NH_4)H_3P_2O_6$ aq. solution	Interpretation	Related frequencies in $P_2O_6^{4-}$ (cm.$^{-1}$)
2252 (3, b)		O–H–O stretching	
1695 (4, v b)		O–H–O deformation	
1339 (5, v sp)		O–H–O deformation	
1186 (10, v sp)	1175 (2, b)	$PO_2(OH)$ stretching	ν_{10}, E_g, 1168
1050 (8, sp)	1069 (6, b)	$PO_2(OH)$ stretching	ν_7, E_u, 1090
1026 (6, sp)		$PO_2(OH)$ stretching	ν_1, A_{1g}, 1060
943 (7, sp)	957 (2, b)	$PO_2(OH)$ stretching	ν_5, A_{2u}, 942
867 (5, sp)			
676 (5, v sp)	651 (5)	$PO_2(OH)$ deformation	ν_2, A_{1g}, 666
513 (7, m)		$PO_2(OH)$ deformation	ν_8, E_u, 495
475 (3, m)	461 (3, b)	$PO_2(OH)$ deformation	
455 (7, m)			
N.I.	278 (6, d)	P–P stretching	ν_3, A_{1g}, 275

* Maximum of intensity scale, 10; v sp, very sharp; sp, sharp; m, medium definition; b, broad; vb, very broad; d, diffuse (Baudler [3]). N.I., not investigated. nm. Nujol mull.

The infrared spectrum of $Na_2H_2P_2O_6$, as anhydrous salt in Nujol mull, reveals no trace of absorption at frequencies above the sharp Nujol band at 2950 cm.$^{-1}$, and hence in the crystal both OH groups must be involved in hydrogen bonding, as they are well known to be in the diacid salt KH_2PO_4. In fact the frequencies (cm.$^{-1}$) of $H_2PO_4^{-1}$ and $H_2P_2O_6^{2-}$ run parallel in the region concerned:

KH_2PO_4 *	2320	1640	1300
$Na_2H_2P_2O_6$	2252	1695	1339

* Miller and Wilkins, *Ind. Eng. Chem. Analyt.*, 1952, **24**, 1253.

If the highest frequency 2252 cm.$^{-1}$ is taken to be due to O–H–O stretching then, according to Lord and Merrifield,[16] the O–O distance should be close to 2·52 Å, as found by neutron diffraction [17] in potassium dihydrogen phosphate.

The frequency at 1186 cm.$^{-1}$ and those below are reasonably to be assigned to modes of vibration within the ion itself. In the last column of Table 3 the frequencies in $P_2O_6^{4-}$ most closely related in type to those of the acid ion are indicated.

It will be seen from Table 3 that at least four of the fundamentals in the infrared and Raman spectra severally lie within 10—20 cm.$^{-1}$ of one another. This close relation can hardly be fortuitous, and when account is taken of the shift of frequency so often consequent upon the change from solution to crystal, and encountered again in the work on $S_2O_6^{2-}$ and $P_2O_6^{4-}$ with proved values of the shifts, it becomes highly probable that the symmetry of the acid ion is such as to allow most of the frequencies to be common to both spectra. It is unfortunate that no polarization properties were recorded for the Raman frequencies.

(2) *The normal ion* $P_2O_6^{4-}$. In normal hypophosphates, containing a quadruply charged anion, the interionic crystal field must be much stronger than that in the dithionates, with only a doubly charged anion. Consequently, the cationic influence upon anionic vibration frequencies is more emphatic in the former salts, and in analysing their spectra and assigning the anionic frequencies to fundamental types it becomes essential

[15] Schwarzenbach and Zure, *Monatsh.*, 1950, **81**, 202.
[16] Lord and Merrifield, *J. Chem. Phys.*, 1953, **21**, 166.
[17] Bacon and Pease, *Proc. Roy. Soc.*, 1953, *A*, **220**, 397.

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always to refer them to the same cation: the sodium cation, in the anhydrous salt $Na_4P_2O_6$, has been so chosen in the present investigation.

Table 4 shows the influence of a variety of cations in salts examined in Nujol mulls upon the non-degenerate infrared active P–O stretching frequency ν_5, which was also observed for the potassium salt $K_4P_2O_6$ in 50% aqueous solution. Cations intrinsically large, or smaller cations enlarged by much water of hydration (Section A), shift the frequency only slightly from its value in solution. The frequencies in Sections B and C, which comprise cations of rare-gas configuration, appear to illustrate mainly increasing frequency caused by decreasing cation radius and therefore increasing crystal field strength; but the actual crystal structure (at present unknown), as well as the possibility of hydrogen bonding between anion and hydration water, no doubt also play their parts. On the contrary, large cations not of rare-gas configuration (Section D) depress the frequency substantially below that observed in solution, possibly owing to incipient covalent linking.

We shall at first assume that the anion $P_2O_6^{4-}$, like dithionate, has the symmetry D_{3d}, and then show that this assumption leads to a consistent scheme of assignments. Of the eleven possible active frequencies, seven have been directly observed, although, as

TABLE 4. *Frequency shifts for* $P_2O_6^{4-}$ *with change of cation.* $K_4P_2O_6$, *in* 50% *solution,* $\nu_5 = 909$ cm.$^{-1}$.

Cation, and water of hydration of the salt (Nujol mulls)	ν_5, A_u (cm.$^{-1}$)	Cation, and water of hydration of the salt (Nujol mulls)	ν_5, A_u (cm.$^{-1}$)
(A) $Co(NH_3)_6Na,4H_2O$	911	(C) Ba_2, anhydrous	917 †
$K_2Na_2,10H_2O$	911 *		901
$Ce(IV),H_2O$	915	$Ca_2,2H_2O$	922 *
$Na_4,10H_2O$	916 *	Mg_2,H_2O	940
(B) K_4, anhydrous	923	(D) Tl_4, anhydrous	873
$Li_4,7H_2O$	929	Ag_4, anhydrous	877
Li_4,H_2O	935	Pb_2, anhydrous	896
Na_4, anhydrous	942		

* From Corbridge and Lowe, *J.*, 1954, 4555. † See text.

mentioned before, two of the three Raman frequencies observed from an aqueous solution of the potassium salt needed confirmation, which, as well as the missing frequencies, was forthcoming from well-defined combination frequencies (Table 5).

Of the highest three frequencies observed in aqueous solution that at 1023 cm.$^{-1}$ is certainly the strongest in the full Raman spectrum and may therefore be at once assigned as ν_1, A_{1g}, the totally symmetric breathing frequency. The infrared frequencies at 1064 and 909 cm.$^{-1}$ are clearly the two stretching frequencies ν_5 and ν_7. In the spectra of solid hypophosphates (Tables 5 and 6) there is abundant evidence (splitting or broadening) that a double degeneracy is removed from the vibrational mode corresponding to the higher frequency, while the lower remains single and sharply defined. The spectrum of barium hypophosphate, $Ba_2P_2O_6$, provides a unique exception to this regularity. Two separate specimens of this salt, one prepared in crystalline condition by adding barium chloride to a mixture of $Na_2H_2P_2O_6$ and sodium acetate in aqueous solution, and the other by neutralizing the acid sodium salt with aqueous barium hydroxide, gave as Nujol mulls, identical spectra, which entirely confirmed the results of Corbridge and Lowe.[18] In these spectra the higher frequency is sharply resolved into a *triplet*, and the lower equally sharply into a *doublet* (Table 6). Without a knowledge of the crystal structure of the salt an explanation can hardly be attempted, but it is not possible for the spectra of a *free* molecule or ion of the composition A_2X_6 to contain a frequency corresponding to a genuine triply degenerate vibrational mode. A large balance of evidence thus favours the assignment of the higher frequency to ν_7, E_u, and of the lower to ν_5, A_{2u}, as in the case of dithionate.

With the aid of the frequencies observed for ν_5 and ν_7 in the infrared spectra of solid

[18] Corbridge and Lowe, *J.*, 1954, 4555.

TABLE 5. *Hypophosphates: Alkali-metal salts. Observed frequencies (cm.$^{-1}$).*

		Infrared spectra.			
$K_4P_2O_6$		$Na_4P_2O_6$ (1) Nujol	$Li_4P_2O_6,7H_2O$	$Li_4P_2O_6,H_2O$	
aq. soln.	Nujol	(2) KBr disc	Nujol	Nujol	Assignment
		2208 (vw)			$\nu_7 + 2\nu_6$ (2214)
		2208 (w)			
		2150 (m)			$\nu_7 + \nu_1$ (2152)
		2150 (m)			
		2114 (m)			$\nu_{10} + \nu_5$
		2105 (m)			
		2010 (s)			$\nu_1 + \nu_5$ (2004)
		2000 (s)			
		1961 (vw)			$\nu_5 + 2\nu_{11}$ (1958)
		1961 (w)			
		—			
		1450 (s)			$\nu_{11} + \nu_5$
		—			
		1420 (s)			$\nu_7 + \nu_{12}$
1064 (10, b)	1075 (10, sp)	1085 (10, b)	1093 (8, v sp)	1080 (10, vb)	ν_7, E_u
	1037 (8, sh)	1083 (10, sp)	1064 (10, sp)		
909 (8, sp)	923 (5, v sp)	942 (8, v sp)	929 (8, v sp)	935 (8, sp)	ν_5, A_{2u}
		942 (7, v sp)			
	879 (sh)		877 (s)	870 (w)	$\nu_2 + \nu_9$
		770 (sh) [1]			$\nu_3 + \nu_8$
		—			
		—			
		710 (m)			$\nu_9 + \nu_{11}$
		568 (10, sp)			ν_6, A_{2u}
		557 (10, sp)			
	N.I.	517 (s)		N.I.	$\nu_9 + \nu_{12}$
		—			
		493 (8, v sp)			ν_8, E_u
		495 (8, v sp)			

Raman spectrum.

$K_4P_2O_6$, aq. soln.	Assignment
1023 ± 5	ν_1, A_{1g}
666 ± 10	ν_2, A_{1g}
ca. 320	ν_{12}, E_g

General notes: see earlier Tables. [1] Observed in both the NaCl and the KBr range.

TABLE 6.

Hypophosphates: Other rare-gas cations.

Salt, examined in Nujol mull	ν_7, (E_u)	ν_5, (A_{2u})
$Mg_2P_2O_6,H_2O$	1094 (10, vb)	940 (8, m)
	1042 (8, sh)	
$Ba_2P_2O_6$	1111 (10, v sp)	
	1081 (10, v sp)	917 (10, v sp)
	1058 (7, v sp)	901 (10, v sp)
CeP_2O_6,H_2O	1080 (10, vb)	915 (5, sp)

Hypophosphates: Non-rare-gas cations.

$Tl_4P_2O_6$	1053 (7, m)	873 (10, v sp)
	1000 (10, m)	
$Pb_2P_2O_6$	1081 (8, sh)	896 (5, v sp)
	1047 (10, sp)	
$Ag_4P_2O_6$	1031 (10, vvb)	877 (9, m)
$Co(NH_3)_6NaP_2O_6,4H_2O$ *	1058 (10, m)	911 (5, sp)

* Observation of the spectrum of $Co(NH_3)_6PO_4,4H_2O$ enabled cationic frequencies to be eliminated from the spectrum of the hypophosphate salt.

$Na_4P_2O_6$ or $K_4P_2O_6$, together with well-defined combination frequencies interpreted by the $g \times u$ rule, we calculate the Raman frequency ν_1 as it would be observed by using the solid salts (Table 7). The substantial upward shift of this Raman frequency is similar to that shown directly by ν_7 (1064 to 1085 cm.$^{-1}$ in the sodium salt) and ν_5 (909 to 942 cm.$^{-1}$ in the

sodium salt) in the change from $K_4P_2O_6$ solution to $Na_4P_2O_6$ solid. In seeking the remaining stretching frequency ν_{10}, which is commonly of weak intensity and is obscured in the observed Raman spectrum, we notice, first, that in the infrared spectrum of $H_2P_2O_6^{2-}$, in addition to frequencies obviously corresponding to ν_5 and ν_7, another occurs (in both infrared and Raman spectra) at 1175—1186 cm.$^{-1}$. Secondly, the highest stretching frequency registered in the infrared spectrum of $P_2O_7^{4-}$ lies at 1152 cm.$^{-1}$. If from the well-defined high-frequency combination terms at 2150, 2110, and 2000 cm.$^{-1}$, each occurring in at least two of the spectra of $P_2O_6^{4-}$, as shown in Table 5, we deduct the infrared frequencies ν_5 and ν_7, we obtain for ν_{10} by the $g \times u$ rule, the possible Raman frequencies 1208 and 1168 cm.$^{-1}$. Of these the latter has been preferred.

The frequencies at 568, 567, and at 493, 495 cm.$^{-1}$ observed in the infrared spectrum of sodium hypophosphate in Nujol mull and KBr disc preparations respectively are without doubt the P–O deformation frequencies ν_6, A_{2u}, and ν_8, E_u. In the infrared (or Raman) spectrum of phosphite HPO_3^{2-} the pair of corresponding deformation frequencies are as shown in Table 8.[19] Since the constitution of phosphite ion in respect to its P–O vibrations

TABLE 7.* *Shifts of the Raman frequency* ν_1, A_{1g}.

	$K_4P_2O_6$		$Na_4P_2O_6$	
Frequencies (cm.$^{-1}$)	50% aq. soln.	Xl. nm.	Xl. nm.	KBr disc
ν_7, obs. IR	1064	1075	1090	1088
ν_5, obs. IR	909	923	942	942
ν_1, obs. R	1023 ($\pm$5)			
$\nu_1 + \nu_7$, obs. IR			2150	2150
$\nu_1 + \nu_5$, obs. IR		*1976*	*2010*	*2000*
ν_1		1053	1060	1062
(Corrected values)			1068	1058

* Xl. nm., crystals in Nujol mull; obs. IR (or R), observed in the infrared (or Raman) spectrum.

TABLE 8.

	Raman	Infrared	
	Na_2HPO_3 in aq. soln. (cm.$^{-1}$)	K_2HPO_3 in aq. soln. (cm.$^{-1}$)	$BaHPO_3$ in Nujol mull (cm.$^{-1}$)
ν_6, E *	459 (m, dp)	465 (m, b)	471 (m) 498 (m)
ν_3, A_1	550 (vw)	567 (m)	591 (m)

* For terminology see Table 1.

must be close to that of a " monomerized " $P_2O_6^{4-}$ ion, it appears reasonable, in the absence of other evidence, to assign ν_6 and ν_8 of the latter to the mean frequencies 562 and 494 cm.$^{-1}$, respectively.

In the Raman spectrum of $K_4P_2O_6$ one of the symmetrical deformation frequencies ν_2, A_{1g} and ν_{11}, E_g is revealed at 666 ($\pm$10) cm.$^{-1}$, and this from its magnitude is almost certainly the higher of the two possible frequencies. The magnitude of the strong combination frequencies at 1450 and 1420 cm.$^{-1}$ in the infrared spectrum of $Na_4P_2O_6$ (as KBr disc preparation) shows without doubt that a stretching frequency must be a constituent of each. Since only the symmetrical rocking frequency ν_9 remains to be assigned in the infrared spectrum and this can hardly lie much higher than 200 cm.$^{-1}$ (in analogy with $S_2O_6^{2-}$), we deduce, in view of the $g \times u$ rule, that the stretching frequencies concerned are limited to ν_5 and ν_7, giving the choice 330 or 487 cm.$^{-1}$, 350 or 508 cm.$^{-1}$ from which to assign the Raman frequencies ν_{11} and ν_{12}. Of these frequencies, the first is evidently ν_{12} observed in the Raman spectrum round 320 cm.$^{-1}$, and we choose the last and highest as the most probable value for the deformation frequency ν_{11}.

The two remaining assignments, the P–P stretching frequency ν_3 in the Raman spectrum, and ν_9 in the infrared spectrum, follow easily from lower summation frequencies,

[19] Masamichi Tsuboi, *J. Amer. Chem. Soc.*, 1957, **79**, 1351.

as indicated in Table 5. A second, and lower, estimate for ν_{12} at 317 cm.$^{-1}$ is deducible from the combination frequency at 517 cm.$^{-1}$ observed only in the spectrum of a Nujol mull preparation of sodium hypophosphate (which gives ν_6 as 568 cm.$^{-1}$) and not in the KBr disc preparation (which gives ν_6 as 557 cm.$^{-1}$). The shift so illustrated between the two modes of observation may reasonably account for the apparent disparity in the values for ν_{12}: Table 9 shows a mean value.

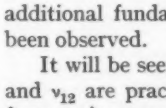
TABLE 9.* *Vibration frequencies* (cm.$^{-1}$).

	$S_2O_6^{2-}$	$P_2O_6^{4-}$		$S_2O_6^{2-}$	$P_2O_6^{4-}$
A_{1g} (Raman)			E_u (Infrared)		
ν_1	1102	1062	ν_7	1240	1085
ν_2	710	670	ν_8	516	494
ν_3	293	275	ν_9	204	200
A_{1u}			E_g (Raman)		
ν_4	—	—	ν_{10}	1216	1168
A_{2u} (Infrared)			ν_{11}	556	508
ν_5	1000	942	ν_{12}	320	323
ν_6	577	562			

In view of the *X*-ray investigations of dithionate the only question about that ion concerns the alternative symmetries D_{3h} and D_{3d}. It appears certain that there are no frequencies common to both Raman and infrared spectra, and all the observed combination frequencies have proved assignable under the $g \times u$ rule. For the symmetry D_{3h} *six binary combination terms, active in the infrared, are allowed which are forbidden for* D_{3d}, namely, $\nu_{7\cdot8\cdot9} + \nu_{8\cdot9\cdot7}$ and $\nu_{10\cdot11\cdot12} + \nu_{11\cdot12\cdot10}$. Of these terms four are calculable from directly observed frequencies: $\nu_7 + \nu_9$ (1756), $\nu_{10} + \nu_{11}$ (1772), $\nu_{11} + \nu_{12}$ (876), and $\nu_{10} + \nu_{12}$ (1536), but no sign of these frequencies occurs, although none of them would be masked by Nujol, water, or fundamental frequencies. The results of the spectral examination thus point strongly to the (staggered) D_{3d} symmetry for dithionate.

While the incompleteness of the observed Raman spectrum of hypophosphate must diminish the force of spectral evidence for its structure, it appears certain that the Raman frequencies ν_1 and ν_2 are absent from the infrared spectrum. In respect to ν_1, this point is made particularly clear by the observation of both spectra (in the NaCl range) on a 50% aqueous solution of potassium hypophosphate, wherein the very intense frequencies ν_1 (1023 cm.$^{-1}$), ν_7 (1064 cm.$^{-1}$) and ν_5 (909 cm.$^{-1}$) are sharply distinguished. In the KBr range there is certainly no fundamental between ν_6 at 562 cm.$^{-1}$ and the usual observational upper limit of the range at 800 cm.$^{-1}$. Structure (I) for $P_2O_6^{4-}$ is thus discredited.

As in the case of dithionate all observed combination terms in the infrared spectrum of hypophosphate conform to the $g \times u$ rule. *Of the six combination terms allowed for* D_{3h} but not for D_{3d} only one, $\nu_7 + \nu_8$ (1584 cm.$^{-1}$), can be calculated from directly observed frequencies, and it certainly does not occur in the infrared spectrum. However, the value of the Raman frequency ν_{10} (1168 cm.$^{-1}$) appears so firmly supported that the absence of the term $\nu_{10} + \nu_{12}$ (near 1500 cm.$^{-1}$) is very probably also significant. The experimental results thus support structure (II) with symmetry D_{3d} for hypophosphate. The forms (I) and (II) do not, however, quite exhaust the structural possibilities for $P_2O_6^{4-}$. There remains a bond diagram (III) (symmetry C_{2h}), which on account of mesomerism could develop a structure of symmetry $D_{2h}(V_h)$. Neither symmetry allows degeneracy, of which for hypophosphate the spectral evidence gives ample proof; it is also very improbable that the two additional fundamentals certain to lie in the infrared NaCl–KBr range would not have been observed.


(III)

It will be seen from Table 9 that while, as is to be expected, the rocking frequencies ν_9 and ν_{12} are practically identical in dithionate and hypophosphate, and the deformation frequencies are only moderately higher for dithionate, the P–O and S–O stretching

frequencies are widely separated. This could be attributed to two major causes: inequality in the intrinsic strengths of P–O and S–O links, and the varying effect of mesomerism acting on the " single " and " double " links in the classical formulæ. The extent of the mesomeric influence can be qualitatively assessed from Table 10, where there is a comparison between the totally symmetrical (breathing) frequencies of oxy-anions of sulphur and phosphorus, which have all been observed under similar conditions in the Raman spectra of aqueous solutions. The formal bond orders, which are simply the

TABLE 10.

Anions	Totally symmetrical S,O stretching frequencies (cm.$^{-1}$)	Formal bond orders	Ref.	Anions	Totally symmetrical P,O stretching frequencies (cm.$^{-1}$)	Formal bond orders	Ref.
$S_2O_6^{2-}$ ...	1092	1·67	1	$H_2PO_2^-$ ...	1048	1·50	3
$S_3O_6^{2-}$ ...	1056		1	$P_2O_6^{4-}$ ...	1023		
$S_4O_6^{2-}$ ...	1042		1	HPO_3^{2-} ...	993	1·33	3
SO_4^{2-}	981	1·50	2	PO_4^{3-} ...	936	1·25	4

(1) Gerding and Eriks, *Rec. Trav. chim.*, 1950, **69**, 724. (2) From closely agreeing results for sodium, potassium, and ammonium sulphates quoted in Kohlrausch, " Der Smekal-Raman Effekt," Springer Verlag, Berlin, 1931. (3) Tsuboi, *J. Amer. Chem. Soc.*, 1957, **79**, 1351. (4) Hoffman and Hanwick, *J. Chem. Phys.*, 1949, **17**, 1166.

ratios $(n_1 + n_2)/n_1$, where n_1 and n_2 are respectively the number of σ- and π-bonds to oxygen in the classical formula, ignore the increase in bond strength ensuing from mesomerism. The true bond orders should be somewhat greater, but will follow the same sequence. A general connexion between frequency and bond order may be inferred in each group of ions, and an inverse relation between frequency and bond length is implied. It is possible to see in the minor frequency differences between polythionate ions and between hypophosphate and phosphite some indications of an interaction between two X–O systems, leading to increasing mesomeric stabilization as the systems come closer together.

On general grounds (*e.g.*, of electronegativity) it would be conjectured that, of P–O and S–O links of similar type and order, the former would be the stronger. The following thermal equations, taken from a recent study,[20] support such a view.

$$(i)\ SOCl_2(g) + \tfrac{1}{2}O_2 = SO_2Cl_2(g):\ \Delta H_{298^\circ} = -35{\cdot}6 \text{ kcal. mole}^{-1}$$

$$(ii)\ PCl_3(g) + \tfrac{1}{2}O_2 = POCl_3(g):\ \Delta H_{298^\circ} = -69{\cdot}1 \text{ kcal. mole}^{-1}$$

There is no significant difference in the S–Cl or S–O bond lengths on the two sides of equation (i), and the P–Cl lengths in PCl_3 and $POCl_3$ are equal.

I am much indebted, not only to Dr. L. A. Woodward for investigating the Raman spectrum of hypophosphate, but also to Dr. N. Sheppard for advising upon and facilitating the observation of the infrared spectra, and to Dr. D. M. Simpson (Mrs. J. N. Agar) for most helpful discussion and criticism.

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[20] Neale and Williams, *J.*, 1952, 4535; 1954, 2156.

305. *The Vapour Pressures of Some Heavy Transition-metal Hexafluorides.*

By George H. Cady and George B. Hargreaves.

The vapour pressures of the hexafluorides of tungsten, molybdenum, rhenium, osmium, and iridium have been measured by a static method using a diaphragm gauge of high sensitivity. Hitherto unknown solid–solid transitions are reported for rhenium, osmium, and iridium hexafluorides together with those known for tungsten and molybdenum hexafluorides. These are, respectively: −1·9°, −0·4°, +0·4°, −8·2°, and −8·7°. From the vapour-pressure data more accurate physical constants, latent heats of vaporisation and sublimation, heats of fusion and transition, and entropies of fusion, transition, and vaporisation have been calculated. Nuclear magnetic resonance studies with both solid and liquid hexafluorides suggest that there is molecular rotation in the solid state above the transition point.

The hexafluorides of tungsten, rhenium, osmium, and iridium (the third-row transition-metal fluorides) have almost the same molecular weights but differ from one another in the number of 5*d*-electrons. Molybdenum is the only second-row element which forms a volatile hexafluoride of which the properties are remarkably similar to those of the heavier rhenium hexafluoride. Low-temperature *X*-ray diffraction measurements on the solids show them to be isostructural and of cubic symmetry.[1]

The vapour pressures of these hexafluorides were first measured by Ruff and his co-workers [2] some time ago. Apart from some recent preliminary measurements with osmium and rhenium hexafluoride [1,3] and a more detailed study of the vapour pressure of liquid tungsten hexafluoride,[4] there have been no further measurements on these compounds, although the handling of elemental fluorine and the improved techniques of preparation have led to much purer products than could have been realized in Ruff's time. With this thought in mind, the vapour pressures of the hexafluorides of tungsten, rhenium, osmium, iridium, and molybdenum have now been measured over considerably greater temperature ranges than those previously recorded. The large temperature intervals over which the previous vapour-pressure measurements were made undoubtedly led the early workers to overlook unknown solid–solid transitions in all of the heavy transition-metal hexafluorides.

Experimental

Vapour-pressure Measurements.—The measurements were made with a Pyrex diaphragm-gauge used as a null intrument (Fig. 1). Previous experience with the handling of transition-metal hexafluorides in Pyrex glass has shown that, providing the apparatus is dry, there is no tendency for the fluorides, even at their b. p., to attack the glass.

The diaphragm gauge, which was of one-piece construction, was connected on the side of the diaphragm away from the sample to a high-vacuum manifold, a mercury manometer, a micro-leak-valve for slowly admitting air when desired, and a mercury diffusion pump. A glass rod of 0·1 mm. diameter and 30 cm. length was sealed at one end to the centre of the diaphragm. It served as a pointer to indicate when the pressures were equal on the two sides of the diaphragm. The gauge was also fitted with two break-seal side-arms. A specimen of the compound to be measured contained in a Pyrex break-seal vessel was glass-blown on to the base of the gauge after a glass-covered breaker had been placed above the seal. The gauge was then pumped under a high vacuum and the glass surfaces above the specimen were flamed for several hours

[1] Weinstock and Malm, *J. Amer. Chem. Soc.*, 1958, **80**, 4466.
[2] Ruff and Tschirch, *Ber.*, 1913, **46**, 929; Ruff and Ascher, *Z. anorg. Chem.*, 1931, **196**, 413; Ruff and Kwasnik, *ibid.*, 1934, **219**, 65; Ruff and Fischer, *ibid.*, 1937, **233**, 282.
[3] Malm, Selig, and Fried, *J. Amer. Chem. Soc.*, 1960, **82**, 1510.
[4] Barber and Cady, *J. Phys. Chem.*, 1956, **60**, 505.

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to remove adsorbed moisture and permanent gases. During this flaming period the volatile hexafluoride was cooled in liquid oxygen. When the gauge and side arms had been adequately baked, the seal connecting the hexafluoride to the diaphragm compartment was broken, and pumping continued for an hour. During this time, the oxygen coolant was removed for a short time to allow a small portion of the hexafluoride to distil out of the gauge. This procedure was adopted so that any traces of silicon tetrafluoride trapped in the specimen would be removed. The compound was again cooled with liquid oxygen, pumping continued for ½ hr., and the gauge sealed at A. The vacuum manifold was then isolated from the mercury diffusion pump.

A 5-l. Dewar vessel which served as the thermostat bath was placed in a position such that the entire gauge except for the upper part of the pointer was immersed in the bath-liquid. For low-temperature measurements (−78·0° to 0·0°) a propyl alcohol–solid carbon dioxide mixture was used. For temperatures between 0·0° and 80·0° water was used as the bath-liquid. The temperature was measured with a calibrated chromel–alumel thermocouple and a portable potentiometer. Temperatures were measured with a precision of 0·05°, and were controlled within 0·1°.

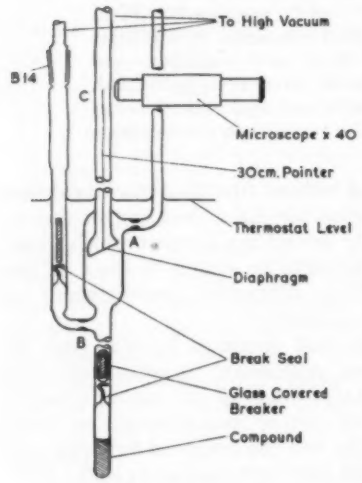

FIG. 1. *Apparatus.*

The position of the pointer was viewed with a Bausch and Lomb travelling microscope, the eye-piece of which contained a calibrated scale. A small bright light-source placed at C facilitated the viewing of the pointer. The mercury manometer was read with a high-precision cathetometer and the pressures were recorded with an accuracy of 0·01 mm. Gauges with sensitivities of 0·10—0·05 mm. were used for the measurements.

The vapour-pressure measurements were made by a null method. The zero point of the gauge was determined with a high vacuum on both sides of the diaphragm. There was no tendency for hysteresis to take place even when the gauge was heated to 400° for several hours. In determining the vapour pressures, the movable pointer was brought back to the zero position by allowing dry air to leak into the ballasted manifold through the micro-leak-valve. The pressure was read directly from the manometer. Vapour-pressure measurements were made with temperatures approached from below and above the desired point.

On completion of an experimental run, a connection was made between the vacuum manifold and one of the break-seal side-arms attached to the part of the system containing the hexafluoride. With equal pressures on each side of the break-seal, the latter was broken and the gauge compartment was pumped while the compound was cooled with liquid oxygen. By removing the liquid oxygen, half of the sample in the gauge was pumped away. The remaining compound was cooled in liquid oxygen, and the gauge re-sealed at B after a short time. The vapour-pressure measurements were then repeated. Concordant results indicated the original material to be of high purity. A third break-seal side-arm (not shown in the Figure) enabled re-entrance to the gauge and allowed dry air to be leaked into the diaphragm compartment in order to equalize the pressure across the diaphragm before removal of the gauge from the vacuum manifold. Several experimental runs were made with different samples of the freshly distilled hexafluoride.

The difficulties experienced by Fairbrother and Frith [5] in the sealing of closed glass systems containing reactive fluorides were not observed with the above apparatus, and no residual gas pressure due to silicon tetrafluoride was found at the completion of an experimental run.

The b. p.s of the five hexafluorides were also determined by use of a standard boiling-point apparatus, the temperature of the vapour in equilibrium with the liquid being measured by a calibrated copper–constantan thermocouple. M. p.s were observed visually during experimental vapour-pressure runs and some transition points were observed from warming-curve data.

[5] Fairbrother and Frith, *J.*, 1951, 3051.

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Materials.—The hexafluorides of tungsten, rhenium, osmium, iridium, and molybdenum were prepared by direct fluorination of the powdered elements in a copper vessel. Fluorine supplied by the General Chemical Division of Allied Chemical and Dye Corporation was used. The gas was diluted with dry oxygen-free nitrogen before passing over the metal. The volatile products were purified by bulb-to-bulb vacuum-distillation and stored at low temperatures over anhydrous sodium fluoride in break-seal vessels.

TABLE 1. *Vapour-pressure equations for* WF_6, ReF_6, OsF_6, IrF_6, *and* MoF_6.

Liquid WF_6 (2·0—17·1°)	Solid WF_6 (−8·2° to 2·0°)	Solid WF_6 (−60° to −8·2°)
$\log P = 7{\cdot}635 - 1380{\cdot}5/T$	$\log P = 8{\cdot}758 - 1689{\cdot}9/T$	$\log P = 9{\cdot}951 - 2006{\cdot}0/T$
Liquid ReF_6 (19·0—33·8°)	Solid ReF_6 (−1·9° to 18·0°)	Solid ReF_6 (−50° to −1·9°)
$\log P = 7{\cdot}732 - 1489{\cdot}1/T$	$\log P = 8{\cdot}539 - 1724{\cdot}7/T$	$\log P = 10{\cdot}110 - 2151{\cdot}2/T$
Liquid OsF_6 (34·0—47·5°)	Solid OsF_6 (−0·4° to 34·0°)	Solid OsF_6 (−40° to −0·4°)
$\log P = 7{\cdot}470 - 1472{\cdot}8/T$	$\log P = 8{\cdot}726 - 1857{\cdot}7/T$	$\log P = 10{\cdot}290 - 2284/T$
Liquid IrF_6 (44·0—54°)	Solid IrF_6 (0·4—44·0°)	Solid IrF_6 (−50·0° to 0·4°)
$\log P = 7{\cdot}952 - 1656{\cdot}5/T$	$\log P = 8{\cdot}618 - 1867{\cdot}5/T$	$\log P = 10{\cdot}000 - 2245{\cdot}7/T$
Liquid MoF_6 (17·4—34°)	Solid MoF_6 (−8·7° to 17·4°)	Solid MoF_6 (−60° to −8·7°)
$\log P = 7{\cdot}766 - 1499{\cdot}9/T$	$\log P = 8{\cdot}533 - 1722{\cdot}9/T$	$\log P = 10{\cdot}216 - 2166{\cdot}5/T$

TABLE 2. *Physical constants of* WF_6, ReF_6, OsF_6, IrF_6, *and* MoF_6.

	B. p. (°c)	Triple pt. (°c)	Triple pt. (mm.)	Transition pt. (°c)	Transition pt. (mm.)	Heat of fusion (cal. mole^{-1})	Entropy of fusion (cal. mole^{-1} deg.$^{-1}$)	Heat of transition (cal. mole^{-1})	Entropy of transition (cal. mole^{-1} deg.$^{-1}$)
WF_6	17·1	2·0	413·2	−8·2	239·9	420	1·45	1400	5·28
ReF_6	33·8	18·7	436·5	−1·9	153·1	940	3·21	2090	7·71
OsF_6	47·5	33·4	474·5	−0·4	81·3	1760	5·72	1970	7·20
IrF_6	53·6	43·8	518·8	+0·4	61·7	1190	3·74	1700	6·21
MoF_6	34·0	17·40	398·1	−8·7	104·7	920	3·15	1960	7·40

TABLE 3. *Latent heats of vaporisation and sublimation, and entropies of vaporisation.*

	Latent heat of vaporisation of liquid (cal. mole^{-1})	Latent heat of sublimation (above transition pt.) (cal. mole^{-1})	Latent heat of sublimation (below transition pt.) (cal. mole^{-1})	Entropy of vaporisation of liquid (cal. mole^{-1} deg.$^{-1}$)
WF_6	6330	7750	9150	21·8
ReF_6	6860	7800	9890	22·3
OsF_6	6720	8480	10,450	21·0
IrF_6	7380	8570	10,270	22·6
MoF_6	6940	7850	9810	22·5

Since the high-temperature fluorination of rhenium metal resulted in the formation of some rhenium heptafluoride,[3] the preparation of rhenium hexafluoride was conducted at as low a temperature as possible. Reduction of the finely powdered metal in hydrogen at red heat before fluorination gave a very reactive surface which burned in fluorine without the application of external heat and little rhenium heptafluoride was formed.

The hexafluorides were further purified by repeated vacuum-distillations over anhydrous sodium fluoride and were finally transferred to break-seal vessels attached to the vacuum-line. These were sealed off under a high vacuum and stored at liquid-oxygen temperature until ready for use.

Some difficulty was experienced in the purification of rhenium hexafluoride and in its separation from the less volatile rhenium heptafluoride. The compound was repeatedly vacuum-distilled at a low temperature, the first fraction and tailings being discarded, until a constant vapour pressure for the product was obtained at the ice point.

Nuclear Magnetic Resonance Spectra.—The nuclear magnetic resonance spectra of both solid and liquid tungsten and molybdenum hexafluorides were obtained through the use of Varian model 4311B high-resolution spectrometer employing a 60 megacycle oscillator. The probe was capable of being heated to 60° or cooled to −30°. Attempts were made to observe the spectra of rhenium, osmium, and iridium hexafluorides by using the variable-temperature probe.

Results.—The vapour-pressure data for the solid and liquid hexafluorides are summarized by the equations in Table 1.

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The equations were derived from the vapour-pressure data, the curve for each phase being considered to be a straight line. The number of vapour-pressure measurements used in determining the relevant equations varied according to the individual compounds. At least ten observations were recorded for all compounds from −78° to the transition points, and a similar number of observations was made for each of the other two phases. Vapour pressures were normally recorded at 3° intervals except when the phase under investigation was of short temperature range. In such circumstances, pressures were recorded at 1° intervals. The maximum deviations of the observed vapour pressures and those calculated from the equations are ±0·5 mm. in the pressure region 0—100 mm. Hg. and ±3 mm. at 760 mm.

The values of the triple points in Table 2 are observed m. p.s and are accurate to 0·2°. The breaks in the vapour-pressure curves were within ±0·2° of the observed triple points. These are tabulated together with heats of fusion and transition, and entropies of fusion and transition. The heats of fusion were derived from the differences between the calculated heat of sublimation and vaporization at the triple point, and the heats of transition from the differences between the heats of sublimation at the transition point. The transition points were obtained from the intersections of the sublimation curves and the values obtained from solution of the vapour-pressure equations were in agreement within ±0·2°.

The heats of sublimation and vaporization, and the entropies of vaporization for the five hexafluorides, are given in Table 3. These were derived by using the Clausius–Clapeyron equation.

Well-defined nuclear magnetic resonance spectra were obtained for tungsten and molybdenum hexafluorides. The former gave a single peak and the latter a large central peak with six small satellite peaks due to molybdenum isotope effects.[6] The same spectra were obtained for the solid hexafluorides as for the liquid phase. Below the transition points the spectra broadened out so much that lines were not observed.

Discussion

The vapour pressure of tungsten hexafluoride was first reported by Ruff and Ascher,[2] and there is good agreement between their results and those reported here, except in the temperature region below the transition point. Ruff and Ascher gave m. p. 2·3° and b. p. 17·5°, but they overlooked the solid–solid transition at −8·2° although their data show evidence for a break in the curve at −8·2°. Barber and Cady [4] later measured the vapour pressure of liquid tungsten hexafluoride from 11·8° to 51·38° with high precision. Their b. p. of 17·05° ± 0·5° is somewhat lower than Ruff and Ascher's value, but is in excellent agreement with ours of 17·1°. From a warming curve of solid tungsten hexafluoride, Barber and Cady observed a solid–solid transition at −8·2° as well as the m. p. at 2·0° ± 0·3°. Their estimated heats of transition and fusion from the warming-curve data, namely, 1600 ± 300 cal. per mole and 500 ± 100 cal. per mole, respectively, are in rather good agreement with the values shown in Table 2. Ruff and Ascher's value of 2400 cal. per mole for the heat of fusion of tungsten hexafluoride is very high, but this is obviously a result of not recognizing the existence of a solid–solid transition at −8·2°.

The vapour pressure of rhenium hexafluoride has been reported by Ruff and Kwasnik [2] who gave a graph but no numerical data. Their b. p. of 47·5° is considerably higher than the value 33·8° now found. This discrepancy has been explained by Malm, Selig, and Fried,[3] who produced a mixture of rhenium hexafluoride with rhenium heptafluoride, the latter being the less volatile of the two, by the high-temperature fluorination of metallic rhenium. The heptafluoride readily formed solid solutions with the hexafluoride, thereby causing the mixture to be less volatile than pure rhenium hexafluoride and we are of the same opinion as Malm, Selig, and Fried, *viz.*, that Ruff and Kwasnik measured the vapour pressure of such a mixture. The preliminary vapour-pressure measurements of pure rhenium hexafluoride reported by Malm *et al.* are in excellent agreement with our data. Our measurements show that rhenium hexafluoride has a solid–solid transition at −1·9°.

The yellow, volatile fluoride of osmium was first reported by Ruff and Tschirch [2] to be

[6] Muetterties and Phillips, *J. Amer. Chem. Soc.*, 1959, **81**, 1084.

the octafluoride OsF_8 with m. p. 34·4° and b. p. 47·5°. The identity of this compound was unchallenged for some 40 years until recent work by Weinstock and Malm [1] disproved the octafluoride and showed the highest fluoride of osmium to be the hexafluoride, a fact further substantiated by Hargreaves and Peacock [7] from magnetic-susceptibility measurements. In the present study the vapour pressure of pure osmium hexafluoride has been measured over a wide temperature range. The data indicate a m. p. of 33·4° and a b. p. of 47·5°, values in good agreement with those of Ruff and Tschirch and of Weinstock and Malm. Ruff and Tschirch measured the vapour pressure of osmium hexafluoride, using the method of Smith and Menzies; consequently, they obtained values only for the liquid

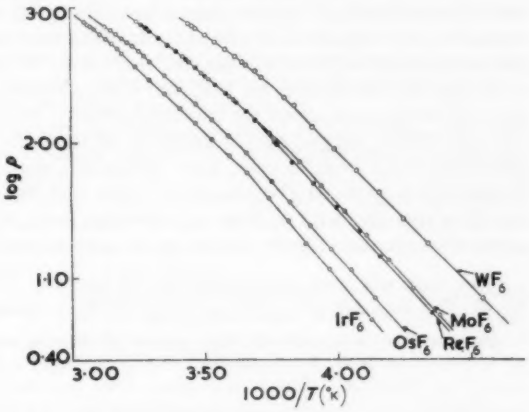

FIG. 2. *Vapour-pressure curves of fluorides.*

hexafluoride. It was not possible for them to observe a triple point or a solid–solid transition from vapour pressures. Our low-temperature data clearly show a solid–solid transition at −0·4°.

The vapour pressure of iridium hexafluoride was first measured by Ruff and Fischer,[2] and there is good agreement between their results and those reported here. However, a direct comparison of results cannot be made because their actual data are not reported. Although Ruff and Fischer report m. p. 44·0°, their vapour-pressure curve does not show a break at the triple point. As with rhenium and osmium hexafluorides, a hitherto unreported solid–solid transition was observed in the present research, the value for IrF_6 being 0·4°.

The vapour pressure of molybdenum hexafluoride has been reported by Ruff and Ascher,[2] and again their results agree with ours. The maximum temperature for which Ruff and Ascher made measurements was 21·0° and their extrapolated b. p. of 35·0° is a little higher than our value, 34·0°. As with tungsten hexafluoride, Ruff and Ascher overlooked a solid–solid transition at −8·7° although their data suggest a break in the curve at this temperature. Brady, Meyers, and Clauss [8] recently measured the heat capacity of molybdenum hexafluoride and reported a solid–solid transition at −9·6°. Their value for the heat of transition of 1960 cal. per mole is in excellent agreement with the value now found, *viz.*, 1957 cal. per mole calculated from the differences in the heats of sublimation at the transition point. The erroneous heat of fusion of 2500 cal. per mole reported by Ruff and Ascher is the result of not realizing the existence of a solid–solid transition. The thermal value, 1059 ± 10 cal./mole, reported by Brady, Meyers, and Clauss is higher than the value, 915 cal./mole, now found.

The physical constants (Table 2) show that the volatilities of solid and liquid WF_6,

[7] Hargreaves and Peacock, *Proc. Chem. Soc.*, 1959, 85.
[8] Brady, Meyers, and Clauss, *J. Phys. Chem.*, 1960, **64**, 588.

ReF_6, OsF_6, and IrF_6 decrease with increase in molecular weight and that the transition and melting points increase. Table 2 and Fig. 2 show the close similarity of the hexafluorides, particularly those of rhenium and molybdenum.

The similar entropies of transition for ReF_6, OsF_6, IrF_6, and MoF_6 suggest a close relation between the entropies of rotation in the solid compounds. The latent heats of vaporization shown in Table 3 increase through the series WF_6, ReF_6, OsF_6, and IrF_6, except that osmium hexafluoride has a slightly lower heat of vaporization than rhenium hexafluoride. The Trouton constants of the liquid hexafluorides are as one would expect for normal liquids.

Little can be said regarding the nuclear magnetic resonance spectra of the transition-metal hexafluorides. Apart from the diamagnetic tungsten and molybdenum hexafluorides, the unpaired 5*d*-electrons in rhenium, osmium, and iridium hexafluorides prevented observation of the fluorine resonances in these compounds in this research.

It was interesting that for WF_6 and MoF_6 a sharp fluorine resonance was obtained with the solid compounds above the transition point. Below this point the sharp peak broadens out completely, suggesting the cessation of molecular rotation. It seems that the solid transition-metal hexafluorides have properties similar to the " liquid-crystal " state at temperatures between the transition point and the triple point. The transition-metal hexafluorides also tend to form a glass-clear mass, which is presumably a single crystal, when they are stored below the m. p. for a considerable time.

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306. *Vapour Pressures of Some Fluorides and Oxyfluorides of Molybdenum, Tungsten, Rhenium, and Osmium.*

By George H. Cady and George B. Hargreaves.

The vapour pressures of the pentafluorides, ReF_5, MoF_5, OsF_5, the oxytetrafluorides, $ReOF_4$, $MoOF_4$, WOF_4, and the oxyfluorides $ReOF_5$ and ReO_2F_3 have been measured by a static method using a diaphragm gauge of high sensitivity. The physical constants, heats of sublimation and vaporisation, and entropies of vaporisation have been derived from the vapour-pressure data. The oxypentafluoride, $ReOF_5$ has been studied in detail and a hitherto unknown solid–solid transition at 30·0° is reported. The thermal disproportionation of the pentafluorides is described.

Within the past four years several new transition-metal fluorides have been prepared and characterised, *e.g.*, platinum hexafluoride,[1] the pentafluorides of molybdenum, rhenium, and osmium,[2,3] and platinum pentafluoride.[4] Tungsten and molybdenum oxytetrafluorides were first described by Ruff *et al.*[5,6] who determined the melting and boiling points of the compounds but not their vapour pressures. Ruff and Kwasnik [7] reported a white rhenium oxytetrafluoride, but later work by Aynsley, Peacock, and Robinson [8] showed the compound to be the oxypentafluoride, $ReOF_5$. The true rhenium oxytetrafluoride

[1] Weinstock, Claassen, and Malm, *J. Amer. Chem. Soc.*, 1957, **79**, 5832.
[2] Hargreaves and Peacock, *J.*, 1960, 1099.
[3] Hargreaves and Peacock, *J.*, 1960, 2618.
[4] Bartlett and Lohmann, *Proc. Chem. Soc.*, 1960, 14.
[5] Ruff, Eisner, and Heller, *Z. anorg. Chem.*, 1907, **52**, 256.
[6] Ruff and Eisner, *Ber.*, 1907, **40**, 2931.
[7] Ruff and Kwasnik, *Z. anorg. Chem.*, 1934, **219**, 65.
[8] Aynsley, Peacock, and Robinson, *J.*, 1950, 1622.

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has been prepared recently by Hargreaves and Peacock.[2] The present paper deals with measurement of the vapour pressures of MoF_5, ReF_5, OsF_5, $MoOF_4$, $ReOF_4$, WOF_4, $ReOF_5$, and ReO_2F_3. Physical constants obtained from the vapour pressures are also given. Boiling points for MoF_5, ReF_5, and OsF_5 have been obtained by extrapolation of vapour-pressure data. These substances disproportionate below their boiling points, so those previously reported are in error.

Experimental

Vapour-pressure measurements were made with a Pyrex diaphragm gauge used as a null instrument (described in the preceding paper).

A UCCO polyethylene glycol bath was used for temperatures up to 200°, and the temperatures were measured with a thermometer reading to 0·1°, the latter being calibrated against a Bureau of Standards thermometer. The mercury manometer was read with a cathetometer with a precision of ±0·05 mm. The sensitivity of the gauge was 0·1 mm. per scale division, so the pressures could be measured with a precision of ±0·1 mm. Hg.

Materials.—The starting materials for the preparation of MoF_5, ReF_5, $ReOF_4$, and OsF_5 were the hexafluorides of molybdenum, rhenium, and osmium, these being prepared by direct fluorination of the powdered metals in a copper vessel. The fluorine, which was diluted with oxygen-free nitrogen, was supplied by General Chemical Division, Allied Chemical and Dye Corporation. The volatile products were purified by bulb-to-bulb vacuum-distillation and stored over anhydrous sodium fluoride in Pyrex break-seal vessels. Tungsten and molybdenum hexacarbonyls were purified by sublimation in a high vacuum.

Molybdenum pentafluoride. This was prepared by Peacock's method.[9] Molybdenum hexacarbonyl was fluorinated at −65° to give the green compound Mo_2F_9 which was then thermally disproportionated at 100° to give molybdenum pentafluoride and the non-volatile molybdenum tetrafluoride. The former sublimed out of the heated zone and was purified by vacuum-sublimation before being transferred to a break-seal vessel. Molybdenum pentafluoride was also prepared by direct interaction of molybdenum hexacarbonyl and molybdenum hexafluoride.[10] A mixture of the pentafluoride and tetrafluoride was obtained, and the former was readily separated from the non-volatile tetrafluoride by vacuum sublimation.

Rhenium pentafluoride and oxytetrafluoride. These were prepared as described by Hargreaves and Peacock.[2] The pentafluoride was obtained by reduction of rhenium hexafluoride with tungsten hexacarbonyl in the presence of tungsten hexafluoride as a solvent. Pure rhenium pentafluoride was readily separated from the reaction mixture by vacuum distillation at 100°. The oxytetrafluoride was prepared in a similar manner by reaction of an excess of rhenium hexafluoride with tungsten hexacarbonyl. After the vigorous reaction the green product was heated to 65° under a high vacuum, to yield blue crystals of rhenium oxytetrafluoride which sublimed out of the heated zone. The compound was purified by vacuum-sublimation and transferred to a break-seal vessel.

Osmium pentafluoride. This was prepared by Hargreaves and Peacock's method.[2] Reduction of osmium hexafluoride with tungsten hexacarbonyl gave a mixture of the pentafluoride and tetrafluoride from which the former was readily separated by vacuum distillation at 120°. The pentafluoride was further purified by vacuum-distillation.

Tungsten and molybdenum oxytetrafluorides. These compounds were prepared by direct fluorination of the powdered metals in the presence of oxygen. A 3 : 1 fluorine–oxygen mixture was used. The oxytetrafluorides were readily separated from any hexafluoride formed simultaneously by pumping under a vacuum at room temperature, the volatile hexafluoride being readily removed. The compounds were then purified by vacuum-sublimation before being transferred to break-seal vessels.

Rhenium oxypentafluoride and dioxytrifluoride. These were prepared by Aynsley, Peacock, and Robinson's method.[8] Rhenium oxypentafluoride was prepared by direct fluorination of rhenium metal in the presence of oxygen. The oxypentafluoride was separated from a small quantity of rhenium hexafluoride, also formed in the reaction, by vacuum-distillation and was purified by repeated vacuum-distillation over sodium fluoride, the fore and tail fractions being discarded. The oxypentafluoride was also prepared by direct fluorination of anhydrous rhenium

[9] Peacock, *Proc. Chem. Soc.*, 1957, 59.
[10] Hargreaves and Peacock, unpublished work.

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dioxide; this method gave rhenium dioxytrifluoride as the major product, but the oxypentafluoride was readily removed owing to its high volatility. Rhenium dioxytrifluoride was purified by vacuum-distillation at 130°.

The m. p.s of MoF_5, ReF_5, OsF_5, and ReO_2F_3 were determined directly in thin-walled Pyrex capillaries. The transition and melting points of $ReOF_5$ were determined from both warming- and cooling-curve data in addition to the values obtained from the vapour-pressure data. The b. p. of $ReOF_5$ was also determined by using a boiling-point apparatus similar to that described by Fairbrother and Frith.[11] The temperature of the vapour in equilibrium with the liquid was measured with a calibrated chromel–alumel thermocouple.

Results.—The vapour-pressure data are summarised by the equations in Table 1. The equations were derived from a minimum of ten observed pressures for each phase. Vapour

TABLE 1. *Vapour-pressure equations.*

Liquid MoF_5 (70·0—160°): $\log P = 8{\cdot}58 - 2772/T$.	
Liquid $MoOF_4$ (95—185°): $\log P = 8{\cdot}716 - 2671/T$.	Solid $MoOF_4$ (40—95°): $\log P = 9{\cdot}21 - 2854/T$.
Liquid ReF_5 (48·0—140°): $\log P = 9{\cdot}024 - 3037/T$.	
Liquid $ReOF_4$ (108—172°): $\log P = 10{\cdot}09 - 3206/T$.	Solid $ReOF_4$ (50—107°): $\log P = 11{\cdot}88 - 3888/T$.
Liquid OsF_5 (75—180°): $\log P = 9{\cdot}75 - 3429/T$.	
Liquid $ReOF_5$ (41—73°): $\log P = 7{\cdot}727 - 1678{\cdot}6/T$.	Solid $ReOF_5$ (30—41°): $\log P = 8{\cdot}620 - 1958{\cdot}9/T$.
Solid $ReOF_5$ (0—30°): $\log P = 9{\cdot}581 - 2250{\cdot}1/T$.	
Liquid ReO_2F_3 (90—170°): $\log P = 10{\cdot}36 - 3437/T$.	
Liquid WOF_4 (105—186°): $\log P = 9{\cdot}69 - 3125/T$.	Solid WOF_4 (50—104°): $\log P = 10{\cdot}96 - 3605/T$.

pressures were normally recorded at 5° intervals except in the case of rhenium oxytetrafluoride, when pressures were recorded at 1° intervals between the transition point and the m. p. The maximum deviations of the observed vapour pressures and those calculated from the equations are ±0·5 mm. at a pressure of 100 mm., ±1 mm. at 400 mm., and ±3 mm. at 760 mm.

The values of the triple points of $MoOF_4$, $ReOF_4$, WOF_4, and $ReOF_5$ were determined by solution of the vapour-pressure equations and are in good agreement (±0·2°) with m. p.s obtained directly in thin-walled capillaries. The m. p.s of MoF_5, ReF_5, OsF_5, and ReO_2F_3 were found to be, respectively, 67·0°, 48·0°, 70·0°, and 90·0°. Owing to the very low vapour pressure of the pentafluorides below the m. p.s, it was not possible to obtain accurate sublimation pressures by using the diaphragm-gauge technique. The solid–solid transition at 30·0° and the m. p. of 40·8° for $ReOF_5$ were obtained from the two plateaux in a warming curve.

Some physical constants of the compounds are shown in Table 2. The heat of fusion was derived from the difference between the heats of sublimation and vaporisation at the triple

TABLE 2. *Physical constants of* MoF_5, ReF_5, OsF_5, WOF_4, $MoOF_4$, $ReOF_4$, $ReOF_5$, *and* ReO_2F_3.

	B. p. (°c)	Triple point (°c)	Triple point (mm.)	Transition point (°c)	Transition point (mm.)	Heat of fusion (cal. mole^{-1})	Entropy of fusion (cal. mole^{-1} deg.$^{-1}$)	Heat of transition (cal. mole^{-1})	Entropy of transition (cal. mole^{-1} deg.$^{-1}$)
MoF_5 ...	213·6	67·0	—	—	—	—	—	—	—
$MoOF_4$ ...	186·0	97·2	28·8	—	—	1020	2·768	—	—
ReF_5 ...	221·3	48·0	—	—	—	—			
$ReOF_4$ ...	171·7	107·8	45·2	—	—	3230	8·478	—	—
OsF_5 ...	225·9	70·0	—	—	—	—	—	—	—
$ReOF_5$ ...	73·0	40·8	237·1	30·0	144·6	1220	3·886	1339	3·868
ReO_2F_3	185·4	90·0	—	—	—	—	—	—	—
WOF_4 ...	185·9	104·7	25·1	—	—	2260	5·981		

point. The heat of transition was derived from the difference between the two heats of sublimation at the transition point. These values are probably not accurate closer than 10 cal. per mole.

The heats of sublimation and vaporisation for $MoOF_4$, $ReOF_4$, WOF_4, and $ReOF_5$, and the

[11] Fairbrother and Frith, *J.*, 1951, 3051.

TABLE 3. *Heats of vaporisation and sublimation and entropies of vaporisation.*

	Heat of vaporisation (cal. mole^{-1})	Heat of sublimation (cal. mole^{-1})	Heat of sublimation below solid–solid transition (cal. mole^{-1})	Entropy of vaporisation (cal. mole^{-1} deg.$^{-1}$)
MoF_5	12,370	—	—	25·4
$MoOF_4$	12,090	13,110	—	26·3
ReF_5	13,880	—	—	28·1
$ReOF_4$	14,590	17,820	—	32·7
OsF_5	15,680	—	—	31·4
$ReOF_5$	7720	8940	10,280	22·3
ReO_2F_5	15,700	—	—	34·3
WOF_4	14,230	16,490	—	31·0
NbF_5	12,900	—	—	25·4 [11]
TaF_5	13,000	—	—	25·9 [11]
IF_5				27·2 [11]
VF_5	10,640	11,940	—	33·1 [11]

heats of vaporisation for MoF_5, ReF_5, OsF_5, and ReO_2F_3 were calculated from the slopes of the lines of the vapour-pressure equations. These values are given in Table 3, together with the entropies of vaporisation for all the liquid states. Table 3 also contains values for NbF_5, TaF_5, IF_5, and VF_5 taken from the literature. These are given to permit comparison of various pentafluorides with each other.

DISCUSSION

Both tungsten and molybdenum oxytetrafluoride have been known for many years. The former was first prepared by Ruff, Eisner, and Heller,[5] and the latter by Ruff and Eisner.[6] The m. p.s of WOF_4 and $MoOF_4$ reported were 110° and 97°, and the b. p.s 185° and 180° respectively. These workers gave no vapour pressures. The physical constants derived from the present vapour-pressure data are in general agreement with those of Ruff *et al.* Their value for the m. p. of tungsten oxytetrafluoride is somewhat higher than the 105° reported here; however, there is excellent agreement in the values of the b. p.s. In a similar manner there is good agreement regarding the m. p. of molybdenum oxytetrafluoride, but the b. p.s do not agree well.

Ruff and Kwasnik [7] described rhenium oxytetrafluoride as a white substance with m. p. 39·7° and b. p. 62·7°. The preparation was repeated by Aynsley, Peacock, and Robinson,[8] who showed that the volatile oxyfluoride prepared by the fluorination of rhenium in the presence of oxygen was the oxypentafluoride $ReOF_5$ and not the oxytetrafluoride $ReOF_4$. The m. p. and b. p. of the oxypentafluoride reported by Aynsley, Peacock, and Robinson were 34·5° and 55·0° respectively. No vapour pressures were given. Ruff and Kwasnik measured the sublimation pressures of their compound, but did not record any data for the liquid state. Their data were published as a graph and it has not been possible to compare their results in detail with those reported here. Rhenium oxypentafluoride has now been studied extensively. In addition to the m. p. of 40·8° and the b. p. of 73·0°, a solid–solid transition has been found to occur at 30·0°. The m. p. of 40·8° reported here is thus in agreement with Ruff's value of 39·7° although the b. p.s differ substantially. Since Ruff and Kwasnik did not record any vapour-pressure measurements above the m. p. of rhenium oxypentafluoride, their extrapolated b. p. of 62·7° could have been in considerable error. The close agreement in the m. p.s suggests that their compound was pure, however, and verifies the conclusions of Aynsley, Peacock, and Robinson that the compound reported by Ruff and Kwasnik to be rhenium oxytetrafluoride was in fact rhenium oxypentafluoride. The rather low values of the physical constants of the oxypentafluoride reported by Aynsley, Peacock, and Robinson are presumably the result of the presence of the more volatile rhenium hexafluoride in their sample of the oxypentafluoride.

Rhenium oxytetrafluoride, a deep blue, readily sublimable solid, was prepared recently by Hargreaves and Peacock.[2] The physical constants reported here show that the

compound has similar properties to those of tungsten and molybdenum oxytetrafluorides. The rhenium compound is considerably more reactive than the tungsten and the molybdenum compound as shown by its attack upon glass at 170° and above. Tungsten and molybdenum oxytetrafluorides had no tendency to attack glass at 186°.

Rhenium dioxytrifluoride was first prepared by Aynsley, Peacock, and Robinson,[8] who reported the liquid to be very viscous, congealing, when cooled, to a glass which crystallised only after long standing. The solid melted at 90—95° and boiled at about 200°. The physical constants were re-investigated by Aynsley and Hair,[12] who reported the m. p. and b. p. to be 95° and 126°, respectively. The physical constants of rhenium dioxytrifluoride reported here and derived from vapour-pressure data are in agreement with the observations of Aynsley, Peacock, and Robinson. The very low b. p. reported by Aynsley and Hair is difficult to explain and is presumably the result of a printing error.

Attempts were made to measure the vapour-pressure of osmium oxytetrafluoride,[3] but in all cases the compound decomposed above about 70°, probably owing to its high reactivity.

The oxytetrafluorides of the third-row transition elements are remarkably similar as shown by the data in Table 2. The chemical reactivity increases with molecular weight. This is further shown by the fact that osmium oxytetrafluoride is very difficult to prepare and iridium oxytetrafluoride has not yet been successfully identified. The data in Table 3 show that there is an increase in both the latent heat and entropy of vaporisation with increase in molecular weight of the compound as one passes from molybdenum to rhenium. The high values of the Trouton constants, particularly for WOF_4 and $ReOF_4$, suggest considerable association in the liquid state.

The three pentafluorides MoF_5, ReF_5, and OsF_5 form an interesting series in that they all undergo irreversible disproportionation at higher temperatures. The diaphragm-guage technique is particularly useful for studying such compounds since the point at which disproportionation takes place can be readily observed from the increase of pressure at constant temperature. The b. p.s of the pentafluorides reported here are extrapolated values. Because of the thermal disproportionation, these values are considered more reliable than those obtained by actually boiling the substances at one atmosphere pressure.

Rhenium pentafluoride undergoes irreversible thermal disproportionation at 130° to give the hexafluoride and the non-volatile tetrafluoride. This particular property of rhenium pentafluoride was used by Hargreaves and Peacock [2] to prepare pure rhenium tetrafluoride. Molybdenum pentafluoride begins to disproportionate at 165°, and osmium pentafluoride at 180°. In each instance, the products of the disproportionation are the volatile hexafluorides and the non-volatile tetrafluorides. This disproportionation can be represented by the general equation: $2MF_5 \longrightarrow MF_6 + MF_4$.

As with the oxytetrafluorides, the heats and entropies of vaporisation of MoF_5, ReF_5, and OsF_5 increase with increase of molecular weight (Table 2). There is also a close similarity in the b. p.s of the compounds. It is pertinent to compare some of the physical properties of MoF_5, ReF_5, and OsF_5 with those of the other pentafluorides shown in Table 3. All the pentafluorides have high Trouton constants, indicative of considerable association in the liquid state. It is now well known that iodine pentafluoride undergoes self ionisation according to the reaction $2IF_5 \longrightarrow IF_4^+ + IF_6^-$. Clark and Emeléus [13] have shown from conductivity measurements that vanadium pentafluoride undergoes a similar type of self-ionisation: $2VF_5 \longrightarrow VF_4^+ + VF_6^-$. In view of the isolation of stable hexafluoromolybdates,[14] hexafluororhenates,[15] and hexafluoro-osmates [16] containing

[13] Aynsley and Hair, *J.*, 1958, 3747.
[13] Clark and Emeléus, *J.*, 1957, 2119.
[11] Hargreaves and Peacock, *J.*, 1957, 4212.
[15] Peacock, *J.*, 1957, 467.
[16] Hepworth, Peacock, and Robinson, *J.*, 1954, 1197.

the MoF_6^-, ReF_6^-, and OsF_6^- ions, it is reasonable to assume that molybdenum, rhenium, and osmium pentafluoride also self-ionise to some extent: $2MF_5 \longrightarrow MF_4^+ + MF_6^-$.

The crystal structure of molybdenum pentafluoride is being investigated by Edwards and Peacock,[17] using single-crystal *X*-ray diffraction. They have found that MoF_5 is monoclinic with two molecules per unit cell, and there are two distinct types of fluorine atom although there is no evidence for a bimolecular species $(MoF_5)_2$. Edwards and Peacock suggest an ionic structure of the type $(MoF_4^+)(MoF_6^-)$, and if this is the case it may be assumed that rhenium and osmium pentafluoride may also have this ionic structure. An ionic structure for the pentafluorides would explain the ready thermal disproportionation of the compounds and also the magnetic properties of rhenium [2] and osmium [3] pentafluoride.

Some physical properties of the fluorides and oxyfluorides of rhenium are compared in Table 4. It is noteworthy that the volatilities depend much more upon the number of

TABLE 4. *Physical constants of some fluorides and oxyfluorides of rhenium.*

	B. p. (°c)	M. p. (°c)	Heat of sublimation (cal. deg.$^{-1}$)	Heat of vaporisation (cal. deg.$^{-1}$)	Entropy of vaporisation (cal. mole^{-1} deg.$^{-1}$)
ReF_6	33·8	18·7	7796	6857	22·3 [a]
$ReOF_5$	73·0	40·8	8940	7720	22·3
$ReOF_4$	171·7	107·8	17,820	14,590	32·7
ReF_5	221·3	48·0	—	13,880	28·1
ReO_2F_3	185·4	90·0	—	15,700	34·3
ReO_3F	—	147·0	—	—	— [12]
ReF_4	Sublimes >300°	—	—	—	— [2]
$ReOF_3$	Non-volatile	—	—	—	—

[a] Preceding paper.

TABLE 5. *Physical constants of known pentafluorides and tetrafluorides of the second- and third-row transition elements.*

	NbF_5 [11]	MoF_5 [9]		RuF_5 [18]			
M. p.	80°	67°		107°			
B. p.	235°	213·6°		313°			
	TaF_5 [12]		ReF_5	OsF_5		PtF_5 [4]	
M. p.	95°		48°	70°		75—76°	
B. p.	229°		221·3°	225·9°		300—305°	
		MoF_4	ReF_4	OsF_4	IrF_4 [19]	PtF_4 [a]	WF_4 [10]
M. p.		—	—	—	106—107°	—	
B. p. ...		—	—	—	300°	—	
Volatility		Non-vol.	Sublimes *in vac.* >300°	Distils *in vac.* >350°		Non-vol.	Non-vol.

[a] Sharpe, *J.*, 1950, 3444.

atoms of fluorine and oxygen per rhenium atom in the molecule than upon whether the atoms are oxygen or whether they are fluorine. The greater the ratio (F + O)/Re, the more volatile the compound. The most volatile substances are ReF_6 and $ReOF_5$. These are followed by the group, ReF_5, $ReOF_4$, and ReO_2F_3, and these by ReO_3F, ReF_4, and $ReOF_3$. In the case of $ReOF_4$ and ReO_2F_3 there is a striking difference in viscosities, the latter compound as a liquid being much more viscous than the former. The decrease in volatility is passing from ReF_6 to ReF_4 suggests appreciable ionic character for the tetrafluoride, as seems to be the case with other transition-metal tetrafluorides.

A comparison of the properties of the known transition-metal pentafluorides and tetrafluorides (Table 5) indicates that iridium tetrafluoride lies in a somewhat anomalous position. This fluoride was first reported by Robinson and Westland; [18] it has m. p. 106—107° and b. p. 300°. Table 5 leads to the conclusion that iridium tetrafluoride has properties which are similar to the third-row pentafluorides rather than the tetrafluorides.

[17] Edwards and Peacock, personal communication.
[18] Robinson and Westland, *J.*, 1956, 4481.

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The transition-metal tetrafluorides so far reported are mostly non-volatile solids, and a more detailed investigation of the above iridium fluoride may show this compound to be iridium pentafluoride. The reduction of iridium hexafluoride[10] with tungsten carbonyl in the presence of tungsten hexafluoride gave a yellow volatile solid with similar properties to those of the compound reported by Robinson and Westland. However, no further studies were made with the product. It may be pointed out that similar reactions involving molybdenum, rhenium, and osmium hexafluorides gave the corresponding transition-metal pentafluorides as the principal products.

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307. *Aromatic Polyfluoro-compounds. Part IX.*[1] *Perfluoro-o-xylene, Perfluoro-p-xylene, and Tetrafluoro-phthalic and -terephthalic Acid.*

By B. Gething, C. R. Patrick, and J. C. Tatlow.

Defluorination of perfluoro-1,2- and -1,4-dimethylcyclohexane by iron at 450—500° has given perfluoro-*o*- and -*p*-xylene respectively. With concentrated sulphuric acid these gave respectively tetrafluoro-phthalic and -terephthalic acid. The former was converted into its anhydride and imide and thence into tetrafluoroanthranilic acid. By decarboxylation each phthalic acid gave the expected tetrafluorobenzene.

This paper describes the preparation of perfluoro-*o*- and -*p*-xylene by defluorination[2,3] of the corresponding perfluoro-alicyclic compounds, perfluoro-1,2- and -1,4-dimethylcyclohexane.[4] These were prepared by the vapour-phase fluorination of *o*- and *p*-xylene respectively with cobalt trifluoride at 300—350° in a stirred reaction vessel.[5] They were defluorinated by passage over iron gauze heated to about 450—500°, giving perfluoro-*o*- and -*p*-xylene, respectively. About 35% of the starting materials were recovered, yields being 40—45% based on that consumed. The yields and ease of formation of these compounds from the respective dimethylcyclohexanes are similar to those of perfluorotoluene from perfluoromethylcyclohexane,[2] and show a considerable improvement over the case of perfluorocyclohexane.[3] Thus it appears that, although the introduction of a tertiary carbon atom into an alicyclic fluorocarbon, as in perfluoromethylcyclohexane, reduces the difficulty of defluorination of the compound, a second tertiary atom, as in the perfluorodimethylcyclohexanes, has little further effect.

The trifluoromethyl groups of perfluoro-*o*- and -*p*-xylene were hydrolysed by fuming sulphuric acid at 150°, to give respectively, in good yield, tetrafluorophthalic and tetrafluoroterephthalic acid. The *o*-acid gave di-*S*-benzylthiouronium and disilver salts, but only a monoanilinium salt, despite the use of an excess of aniline. Tetrafluoroterephthalic acid gave di-salts with the same three bases and also a dimethyl ester.

Tetrafluorophthalic acid was converted into its anhydride by treatment with trifluoroacetic anhydride. Unlike phthalic anhydride, tetrafluorophthalic anhydride reacted readily with water. It dissolved almost instantaneously to give a solution that could be titrated with alkali just as though it were one of the free acid. The ease of hydrolysis

[1] Part VIII, Barbour, Buxton, Coe, Stephens, and Tatlow, *J.*, 1961, 808.
[2] Gething, Patrick, Stacey, and Tatlow, *Nature*, 1959, **183**, 588.
[3] Coe, Patrick, and Tatlow, *Tetrahedron*, 1960, **9**, 240.
[4] Fowler, Burford, Hamilton, Sweet, Weber, Kasper, and Litant, *Ind. Eng. Chem.*, 1947, **39**, 292.
[5] Stacey and Tatlow, "Advances in Fluorine Chemistry," Butterworths, London, Vol. I, 1960, p. 166.

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of this anhydride parallels the rapidity of the hydrolysis of anhydrides of aliphatic perfluoro-acids, such as trifluoroacetic anhydride. Perfluoro-aromatic acids also should be strong acids [pentafluorobenzoic acid has a high dissociation constant (pK 0·8) [6]], and the ready hydrolysis of tetrafluorophthalic anhydride is in keeping with the high strength of the acid from which it is derived, the carbon atoms of the carbonyl groups being susceptible to attack by nucleophilic reagents. With ammonia, tetrafluorophthalic anhydride gave tetrafluorophthalimide. As is generally the case with amides, this was less readily hydrolysed than was the related anhydride. Tetrafluorophthalimide was converted into the xanthhydrol derivative and also, by the action of sodium hypobromite, into 3,4,5,6-tetrafluoroanthranilic acid.

By the action of heat on tetrafluorophthalic acid, and on tetrafluoroterephthalic acid, in admixture with soda lime, 1,2,3,4- and 1,2,4,5-tetrafluorobenzene, respectively, were obtained in good yield. These were characterised by infrared spectroscopy and their formation confirms that there had been no migration of substituent groups in the sequence of reactions from the hydrocarbon starting materials. In view of the value of bromo-aromatic compounds in synthetic work an attempt was made to convert the disilver salts of the tetrafluorophthalic acids into the corresponding dibromotetrafluorobenzenes by the Hunsdiecker reaction with bromine; this type of conversion has been very useful in the perfluoro-aliphatic series. However, when the reaction mixtures were worked up, only the appropriate tetrafluorophthalic acid could be isolated. In this process,[7] disilver phthalate gave very little dibromide, some acid being recovered, whilst disilver terephthalate was virtually unattacked.

Experimental

*Preparation of Perfluoro-*o*- and -*p*-xylene.*—Perfluoro-1,2-dimethylcyclohexane (9 g.) was passed in a stream of nitrogen flowing at 2 l./hr. through the defluorination tube [2,3] which was heated to 460°. The product (6 g.) was separated by preparative-scale gas chromatography [8] (column A, temp. 110°) to give starting material (3·1 g.) and *perfluoro-*o*-xylene* (1·8 g.), b. p. 128°, n_D^{19} 1·3670 (Found: C, 33·2; F, 66·2. C_8F_{10} requires C, 33·6; F, 66·4%). Mass spectrometry: principal mass peaks: 286, C_8F_{10}; 267, C_8F_9; 217, C_7F_7. Light absorption in ethanol (c, 0·085 g./l.): $\lambda_{max.}$ 2720 (ε 1753).

Perfluoro-1,4-dimethylcyclohexane (9·0 g.) was treated as described above (reactor temperature 460°, the value quoted earlier [2] should also have been 460°). The product (6·0 g.), separated as before, gave starting material (3·5 g.) and perfluoro-*p*-xylene (1·65 g.), b. p. 122°, n_D^{17} 1·3621 (Found: C, 33·9; F, 66·3%). Light absorption in ethanol (c, 0·047 g./l.): $\lambda_{max.}$ 2850 (ε 2590).

Preparation of Tetrafluorophthalic Acid.—Perfluoro-*o*-xylene (6·4 g.) and fuming sulphuric acid (20% of sulphur trioxide; 4 ml.) were heated at 150° and shaken in a sealed tube for 12 hr. The tube was cooled in liquid air, then opened, and its contents were poured on ice. The resulting solution was made alkaline, extracted with ether, and acidified. The acid solution was extracted continuously with ether for 12 hr. and the extract was decolorised (charcoal), dried ($MgSO_4$), and evaporated to leave a white solid (5·8 g.), m. p. 151—153°, which was recrystallised from *o*-xylene to give *tetrafluorophthalic acid* (5·0 g.), m. p. 153—154° (Found: C, 40·3; H, 1·0; F, 31·6%; equiv., 117. $C_8H_2F_4O_4$ requires C, 40·3; H, 0·8; F, 31·9%; equiv., 119). The infrared spectrum showed a strong band at 1735 cm.$^{-1}$ (C=O).

The acid (0·3 g.) gave in the usual way *di-*(S-*benzylthiouronium*) *tetrafluorophthalate* (0·2 g.), m. p. 205° (decomp.) (from water) (Found: C, 50·8; H, 4·0; F, 13·4. $C_{24}H_{22}F_4N_4O_4S_2$ requires C, 50·5; H, 3·9; F, 13·3%). Treatment of the acid (0·2 g.) with an excess of aniline in ether in the usual way gave *anilinium hydrogen tetrafluorophthalate* (0·2 g.), m. p. 204—205° (decomp.) (from acetone–chloroform) (Found: C, 50·8; H, 2·9. $C_{14}H_9F_4NO_4$ requires C, 50·8; H, 2·7%). A solution of tetrafluorophthalic acid (5·5 g.) in water (20 ml.) was neutralised with aqueous

[6] Alsop, Burdon, and Tatlow, unpublished work.
[7] Oldham, *J.*, 1950, 100.
[8] Stephens, Tatlow, and Wiseman, *J.*, 1959, 148.

sodium carbonate. A solution of silver nitrate (20 g.) in water (50 ml.) was added and the precipitated *disilver salt* (9·5 g.) filtered off (Found: C, 21·4. $C_8Ag_2F_4O_4$ requires C, 21·2%).

Tetrafluorophthalic Anhydride.—Tetrafluorophthalic acid (2·4 g.) was refluxed with trifluoroacetic anhydride (5 ml.) for 2 hr. Trifluoroacetic acid and trifluoroacetic anhydride were removed by distillation under reduced pressure, and the residue was sublimed at 80°/0·05 mm., to yield *tetrafluorophthalic anhydride* (2·0 g.), m. p. 94—95·5° (Found: C, 43·4%; equiv., 110. $C_8F_4O_3$ requires C, 43·6%; equiv., 110). The infrared spectrum showed a band at 1805 cm.$^{-1}$ (C=O).

Tetrafluorophthalimide.—The temperature of a mixture of tetrafluorophthalic anhydride (2·5 g.) and aqueous ammonia (*d* 0·88; 3 ml.) was gradually increased to 280° during 1 hr. The solid product (2·5 g.) sublimed at 120°/0·05 mm., to give *tetrafluorophthalimide* (1·5 g.), m. p. 210—211° (Found: C, 44·2; H, 0·8; F, 34·5. $C_8HF_4NO_2$ requires C, 43·8; H, 0·5; F, 34·7%).

This imide (0·3 g.) was added to a solution of xanthhydrol (0·3 g.) in glacial acetic acid (3 ml.) and heated in a boiling water bath for 30 min. The precipitate was recrystallised from dioxan–water (3 : 2) to give the *derivative* (0·15 g.), m. p. 255—256° (Found: C, 63·3; H, 2·3. $C_{21}H_9F_4O_3N$ requires C, 63·2; H, 2·3%).

Preparation of 3,4,5,6-*Tetrafluoroanthranilic Acid.*—To a cooled solution of sodium hydroxide (1·7 g.) and bromine (1·3 g.) in water (10 ml.) was added finely powdered tetrafluorophthalimide (1·7 g.). A solution of sodium hydroxide (1·1 g.) in water (5 ml.) was added rapidly and the resulting solution heated to 80° for 1 min. and then cooled to 15°. The solution was acidified with concentrated hydrochloric acid, and the resulting precipitate (1·0 g.), m. p. 135—139°, removed by filtration. Reprecipitation from alkaline solution and recrystallisation from water gave 3,4,5,6-*tetrafluoroanthranilic acid* (0·5 g.), m. p. 141—142° (Found: C, 40·5; H, 1·6. $C_7H_3F_4NO_2$ requires C, 40·2; H, 1·4%). The infrared spectrum showed bands at 1675 (C=O), 3400, 3620 (N–H), and 3000 cm.$^{-1}$ broad (O–H).

The acid (0·2 g.) gave in the usual way S-*benzylthiouronium* 3,4,5,6-*tetrafluoroanthranilate* (0·15 g.), m. p. 205° (Found: C, 48·2; H, 3·7. $C_{15}H_{13}F_4N_3O_2S$ requires C, 48·0; H, 3·5%).

Tetrafluoroterephthalic Acid.—Perfluoro-*p*-xylene (6·0 g.) was treated with concentrated sulphuric acid (6 ml.) as for its isomer. Recrystallisation from water of the solid obtained gave *tetrafluoroterephthalic acid* (4·0 g.), m. p. 283—284° (Found: C, 40·2; H, 0·7; F, 31·5%), $\nu_{max.}$ 1725s cm.$^{-1}$ (C=O).

The acid (0·2 g.) gave a *di*-(S-*benzylthiouronium*) *salt* (0·3 g.), m. p. 211—212° (Found: C, 50·7; H, 4·1%).

With aniline in ether the acid (0·26 g.) afforded a *dianilinium salt* (0·20 g.) (from acetone–chloroform), m. p. 205° (decomp.) (Found: C, 56·6; H, 3·6. $C_{20}H_{16}F_4N_2O_4$ requires C, 56·6; H, 3·8%).

Disilver tetrafluoroterephthalate was prepared as was its isomer (Found: C, 21·1%).

The acid (1·1 g.) and concentrated sulphuric acid (1·0 ml.) were refluxed for 5 hr. in methanol (10 ml.). When cooled, the precipitate which formed was filtered off and recrystallised from methanol to give *dimethyl tetrafluoroterephthalate* (0·7 g.), m. p. 79—80° (Found: C, 45·4; H, 2·0. $C_{10}H_6F_4O_4$ requires C, 45·1; H, 2·3%).

Decarboxylations of the Tetrafluorophthalic Acids.—Tetrafluorophthalic acid (0·43 g.) and soda-lime (1·0 g.) were mixed intimately and the temperature increased gradually to 300°. The distillate (0·20 g.) was shown by infrared spectroscopy to be 1,2,3,4-tetrafluorobenzene.[9,9]

In an analogous fashion, tetrafluoroterephthalic acid (0·51 g.) afforded 1,2,4,5-tetrafluorobenzene [10] (0·22 g.) with a correct infrared spectrum.

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[9] Pummer, Florin, and Wall, *J. Res. Nat. Bur. Stand.*, 1959, **62**, 113.
[10] Finger, Reed, Burness, Fort, and Blough, *J. Amer. Chem. Soc.*, 1951, **73**, 145.

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308. *The Epimerization of 2-Acetamido-2-deoxy-D-pentoses.*[1]

By Bruce Coxon and L. Hough.

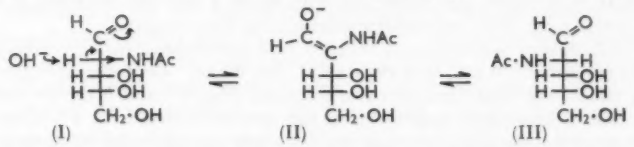
2-Acetamido-2-deoxy-D-ribose and -D-arabinose are equilibrated in aqueous ammonia, an effect ascribed to enolisation of the 2-hydrogen atom of the open-chain form under the influence of the acetamido-group.

The Lobry de Bruyn–Alberda van Ekenstein isomerization of reducing sugars in dilute base [2] proceeds through intermediary enediols. Thus, one carbon-bound deuterium atom is introduced into glucose in alkaline heavy water.[3] Reaction of 2-acetamido-2-deoxy-aldoses [4,5] is not complicated by the formation of 2-ketoses or 2-ketimines, in contrast to that of normal aldoses and 2-amino-2-deoxyaldoses. Rapid equilibration of 2-acetamido-2-deoxy-D-glucose or -mannose in dilute aqueous base was observed to give in each case a mixture containing these epimers in the proportion ~4 : 1 respectively.[4]

When 2-acetamido-2-deoxy-D-ribose [6] (I), $[\alpha]_D$ −36°, was dissolved in dilute aqueous ammonia at 21°, the specific rotation decreased to −59° in 12 hr., and then slowly increased. Paper chromatography of the mixtures at various times suggested that 2-acetamido-2-deoxy-D-arabinose (III) was formed, and that equilibration was complete after about 48 hr., giving a proportion of about 2 : 1 of D-*arabino*- to D-*ribo*-epimer. The major product was separated and characterized as 2-acetamido-2-deoxy-D-arabinose (III), $[\alpha]_D$ −94°.[6,7] This monosaccharide gave a similar mixture in dilute aqueous ammonia, showing that the epimerization was a true equilibration.

The above discrepancy between the rotational evidence and the paper-chromatographic results for the maximum concentration of epimer, is probably due to side-reactions, and paper chromatography of an epimerized reaction mixture after 8 days revealed extensive degradation to other products.

In a comparative experiment, the epimerization of D-ribose to D-arabinose and D-*erythro*-pentulose was insignificant and hence the epimerization is facilitated by the acetamido-group. The rate-determining step in this process is the rate of ionization of the 2-hydrogen atom, which leads to the enolate ion (II). The electrophilic inductive



effect of the acetamido-group is greater than that of the hydroxyl group by virtue of the fractional positive charge on the nitrogen atom which is produced by mesomerism [cf. acetamidoacetic acid (pK 3·65) which is a stronger acid than glycollic acid (pK 3·83) [8]]. Thus, the 2-acetamido-2-deoxy-aldoses will epimerize *via* the acyclic form (*e.g.*, I) and the electron-attracting effect of the acetamido-group will accelerate the ionization of the 2-hydrogen atom and hence increase the rate of formation of the enolate anion (*e.g.*, II), with consequent destruction of asymmetry at position 2 and later formation of the two epimers.

[1] For a preliminary communication, see Coxon and Hough, *Chem. and Ind.*, 1960, 374.
[2] Lobry de Bruyn and Alberda van Ekenstein, *Rec. Trav. chim.*, 1895, **14**, 156, 203; 1896, **15**, 92; 1897, **16**, 241, 257, 262, 274, 282; 1899, **18**, 147; 1900, **19**, 1; Wolfrom and Lewis, *J. Amer. Chem. Soc.*, 1928, **50**, 837.
[3] Sowden and Schaffer, *J. Amer. Chem. Soc.*, 1952, **74**, 505.
[4] Comb and Roseman, *J. Amer. Chem. Soc.*, 1958, **80**, 3166; Spivak and Roseman, *ibid.*, 1959, **81**, 2403.
[5] Brug and Paerels, *Nature*, 1958, **182**, 1159.
[6] Coxon and Hough, *Chem. and Ind.*, 1959, 1249; Kuhn and Baschang, *Annalen*, 1959, **628**, 193.
[7] Baer and Fischer, *J. Amer. Chem. Soc.*, 1960, **82**, 3709.
[8] "International Critical Tables," McGraw-Hill Book Co., New York, 1929, Vol. VI, p. 259.

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Although the rate of carbanion formation is not necessarily linearly correlated with the acidic dissociation constant of the ionizing proton,[9] the idea is well substantiated that electrophilic substituents on a carbon atom to which a potentially acidic hydrogen is attached can increase the rate of carbanion formation. Thus, Hine *et al.*[10] found that deuterochloroform underwent base-catalysed exchange of deuterium for hydrogen about as readily as did deuterated acetaldehyde and acetone.

With 2-acetamido-2-deoxy-pentoses and -hexoses, although the epimerization will proceed *via* the acyclic forms, the resting state of the molecules will probably be the pyranose ring form.[11] Hence the proportion of each epimer in the equilibrium mixture will be governed by the relative stabilities of their pyranose chair conformations.[1]

Experimental

Evaporations were under reduced pressure. Paper chromatography was performed by the descending method at room temperature on Whatman No. 1 filter paper with butan-1-ol–pyridine–water (10 : 3 : 3 v/v) as mobile phase. The following sprays were used: *a*, 0·02M-sodium metaperiodate followed after 5 min. by 4% w/v ammoniacal silver nitrate reagent (for detection of polyols); *b*, *p*-anisidine hydrochloride in butan-1-ol–ethanol–water;[12] *c*, Elson–Morgan reagents.[13] Rates of movement of compounds are quoted relative to that of rhamnose (R_{Rh}) or the solvent front (R_F). M. p.s were determined on a Kofler micro-heating stage. Infrared absorption maxima are for Nujol mulls.

Preliminary Investigation of the Effect of Dilute Aqueous Ammonia on 2-Acetamido-2-deoxy-D-ribose.—A solution of 2-acetamido-2-deoxy-D-ribose (0·116 g.) in 0·73N-aqueous ammonia (10·0 ml.) was examined at various tines (*t*) by polarimetry and by paper chromatography. The specific rotation (calculated as 2-acetamido-2-deoxy-pentose) changed as follows:

t (hr.) ...	0·08	0·5	1·5	2·5	3·5	5·5	11·0	24·0	48·0	72·0	108·0
$[\alpha]_D^{21}$ ...	−40·1°	−41·6°	−45·7°	−48·5°	−51·6°	−56·1°	−58·9°	−55·2°	−50·0°	−45·7°	−41·2°

Paper chromatography after 2 hr. revealed that, in addition to 2-acetamido-2-deoxy-D-ribose (R_{Rh} 1·0), a slower-moving reducing sugar was present which had R_{Rh} 0·78 [sprays *a* and *b* (orange spot)]. The latter spot rapidly increased in intensity and reached a maximum after *ca.* 48 hr. Meanwhile, the intensity of the spot corresponding to 2-acetamido-2-deoxy-D-ribose diminished in intensity until it was *ca.* half that of the other. After 48 hr. a streak of slower-moving degradation products was detectable with spray *a* and this increased in intensity until after 8 days, it was clear that considerable degradation had occurred.

2-Acetamido-2-deoxy-D-arabinose.—A solution of 2-acetamido-2-deoxy-D-ribose (0·163 g.) in 0·73N-aqueous ammonia (10 ml.) was kept at 21° for 96 hr. Concentration then gave a pale yellow syrup, which was separated into two fractions (R_{Rh} 1·0 and 0·78) by chromatography on Whatman 540 (acid-washed) paper run in the pyridine solvent for 4·5 days. Zones were detected with spray *b*; the faster-moving one (R_{Rh} 1·0) corresponded to starting material and was not further investigated; the slower-moving zone (R_{Rh} 0·78) was eluted with methanol (Soxhlet) for 18 hr. and concentration of the eluate then gave a syrup (0·068 g.) which crystallized from methanol–ether, yielding hexagonal plates of 2-acetamido-2-deoxy-D-arabinose (0·033 g.), m. p. 158—160°. Recrystallized from methanol–ether and washed with methanol, they had m. p. 161—163°, $[\alpha]_D^{27}$ −102° (5·5 min.) ⟶ −94° (final; 15 min.; *c* 1·04 in water), R_P 0·34 [sprays *a*, *b* (orange), and *c* (purple)] (Found: C, 43·7; H, 7·0; N, 7·3; Ac, 15·6. Calc. for $C_7H_{13}O_5N$: C, 44·0; H, 6·9; N, 7·3; Ac, 22·5%), $\nu_{max.}$ 3430m, 3300m (OH), 3220w, 1550m (NH), 1645s (*N*-Ac). Baer and Fischer [7] give m. p. 159—160° (decomp.), $[\alpha]_D$ −138° (2 min.) ⟶ −97·3° (30 min.). Kuhn and Baschang [6] record m. p. 160—163°, $[\alpha]_D$ −149° ⟶ 97° (2 hr.).

Effect of Dilute Aqueous Ammonia on 2-Acetamido-2-deoxy-D-arabinose.—2-Acetamido-2-deoxy-D-arabinose (2·5 mg.) was dissolved in 0·73N-aqueous ammonia (0·15 ml.) and kept at 21°. Paper chromatography after 12 hr. revealed 2-acetamido-2-deoxy-D-ribose (R_{Rh} 1·0) in addition to starting material. The intensity of the spot corresponding to the former slowly

[9] Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1956, p. 227.
[10] Hine, Peek, and Oakes, *J. Amer. Chem. Soc.*, 1954, **76**, 827.
[11] Ferrier and Overend, *Quart. Rev.*, 1959, **13**, 272.
[12] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[13] Kent and Whitehouse, "Biochemistry of the Amino-sugars," Butterworths, London, 1955, 164, and references therein.

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increased to *ca.* one-half of that of the spot due to the starting material. After *ca.* 40 hr. an equilibrated mixture of the *ribo*- and *arabino*-derivatives was obtained, similar to that prepared by the action of dilute aqueous ammonia on 2-acetamido-2-deoxy-D-ribose.

Effect of Dilute Aqueous Ammonia on D-*Ribose.*—D-Ribose (0·163 g.) was dissolved in 0·73N-aqueous ammonia (10·0 ml.), and the solution was kept at 21° and examined at intervals by polarimetry and paper chromatography. The specific rotation (calc. as pentose) changed slightly in a direction opposite to that of the equilibrium value (−106°) of D-arabinose:[14]

t (hr.)	0	2	23	49	96	624
$[\alpha]_D^{21}$	−20°	−20°	−20°	−20°	−19°	−17°

D-Arabinose was not detectable on paper chromatograms with spray *b* after 50, 72, and 96 hr. There was, however, a very faint streak towards the starting line, presumably due to degradation products.

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[14] Hough and Taylor, *J.*, 1956, 970.

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309. *Oxidations of Organic Compounds by Cupric Salts. Part II.*[1] *The Oxidation of Benzoin.*

By B. A. MARSHALL and WILLIAM A. WATERS.

The kinetics of the oxidation of benzoin by alkaline cupric citrate resembles that for the oxidation of acetoin: the oxidation step is slower than the base-catalysed enolisation of benzoin. These results substantiate the reaction mechanisms suggested in Part I.

IN Part I [1] it was shown that the oxidations of acetoin by two alkaline cupric salts were preceded by an induction period and thereafter were of zero order with respect to $[Cu^{2+}]$ but of first order with respect to both [acetoin] and $[OH^-]$. It was suggested that the acetoin was oxidised in the form of its enol anion, *E*, the rate-determining stage being, not the slow forward step of the enolisation (1), but a still slower bimolecular reaction (4) which produced a cuprous chelate complex, *C*, which was then attacked by cupric ions. Parentheses, *e.g.*, (Cu^+), (Cu^{2+}), were used in this scheme to indicate that the copper ions involved in these reactions are linked to co-ordinating groups, *e.g.*, citrate or malate: consequently reaction (4) represents the displacement of one chelating group by another.

By concluding that (*C*) and not (*E*) was attacked by cupric ions it was possible to explain the occurrence of an induction period in which cuprous ions are very slowly being formed by way of the radical structure (*R*) which, as equilibrium (8) shows, can have some cupric character.

If the enolisation (1) were the rate-determining reaction then the oxidation would promptly set in at its full velocity and the measured oxidation rate would be equal to, and not less than, the enolisation rate. We now present further evidence in support of our reaction mechanism.

The stoicheiometric oxidation of benzoin to benzil by cupric citrate in the presence of an excess of sodium carbonate has been examined in 40% aqueous dioxan and has all the kinetic features reported in Part I for the oxidation of acetoin. The oxidation has an induction period, which (compare Figs. 3 and 4 of Part I) can in part be eliminated by

[1] Part I, Marshall and Waters, *J.*, 1960, 2392.

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operating under nitrogen and thus preventing any regeneration of cupric ions by autoxidations, such as (7), of the ene-diol complex *C*. Following the induction period, the oxidation is of zero order with respect to $[Cu^{2+}]$.

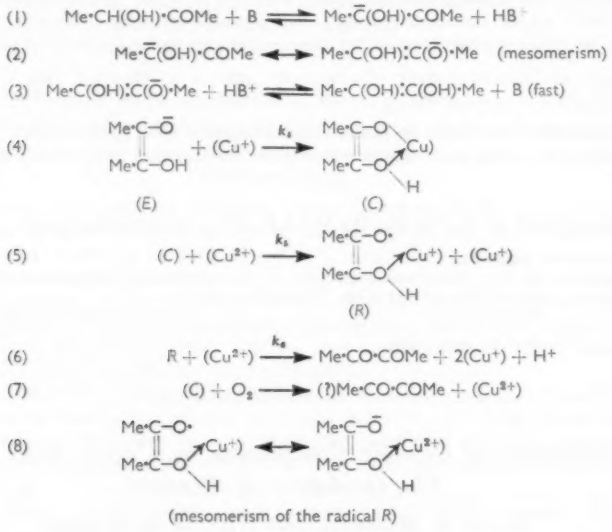
(1) Me·CH(OH)·COMe + B ⇌ Me·C̄(OH)·COMe + HB⁺
(2) Me·C̄(OH)·COMe ⟷ Me·C(OH):C(Ō)·Me (mesomerism)
(3) Me·C(OH):C(Ō)·Me + HB⁺ ⇌ Me·C(OH):C(OH)·Me + B (fast)
(4) + (Cu⁺) k_4
(E)
(C)
(5) (C) + (Cu²⁺) k_5 + (Cu⁺) + (Cu⁺)
(R)
(6) R + (Cu²⁺) k_6 Me·CO·COMe + 2(Cu⁺) + H⁺
(7) (C) + O₂ (?)Me·CO·COMe + (Cu²⁺)
(8)
(mesomerism of the radical R)

Table 1 shows that the oxidation is of first order with respect to [Benzoin]; Table 2 shows that the oxidation is of first order with respect to $[CO_3^{2-}]$ at low carbonate con-

TABLE 1. *Oxidation of benzoin with* Cu^{2+} *at* 30°.

[Each solution contained 0·005M-copper sulphate, 0·03M-sodium citrate, and 0·15M-potassium carbonate in 40% (v/v) dioxan–water.]

[Benzoin] (10^{-2}M)	0·75	1·00	1·25	1·50	1·75	2·00
$10^4 \times -d[Cu^{2+}]/dt$ (mole $l.^{-1}$ $min.^{-1}$)	0·84	1·08	1·60	1·86	2·16	2·35
$10^2 \times$ Rate/[Benzoin]	1·11	1·08	1·28	1·24	1·23	1·17

TABLE 2. *Dependence of oxidation rate on potassium carbonate concentration.*

(Each solution contained 0·005M-copper sulphate, 0·03M-sodium citrate, and 0·02M-benzoin.)

K_2CO_3 (10^{-2}M)	$10^4 \times -d[Cu^{2+}]/dt$ (mole $l.^{-1}$ $min.^{-1}$)	$10^2 \times$ Rate/$[K_2CO_3]$ ($min.^{-1}$)	K_2CO_3 (10^{-2}M)	$10^4 \times -d[Cu^{2+}]/dt$ (mole $l.^{-1}$ $min.^{-1}$)	$10^2 \times$ Rate/$[K_2CO_3]$ ($min.^{-1}$)
2·50	0·51	2·04	10·00	1·80	1·80
3·75	0·69	1·84	11·25	2·04	1·81
5·00	0·99	1·98	12·50	2·10	1·68
6·25	1·24	1·98	13·75	2·21	1·61
7·50	1·47	1·96	15·00	2·35	1·57
8·75	1·66	1·90	17·50	2·55	1·46

centrations, but departs from this at high carbonate concentrations; and Table 3 shows that for carbonate–bicarbonate mixtures the reaction velocity depends on $[OH^-]$ and not on $[CO_3^{2-}]$. These observations are in accord with those of Weissberger, Schwarze, and Mainz,[2] who oxidised benzoin in aqueous alcohol with Fehling's solution. Whereas we have regularly taken [Benzoin] in large excess over $[Cu^{2+}]$, these workers took $[Cu^{2+}]$ in excess and then, naturally, found that the reaction was of first order with respect to $[Cu^{2+}]$, though independent of the initial concentration of the copper salt, for under their

[2] Weissberger, Schwarze, and Mainz, *Annalen*, 1930, **481**, 68.

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conditions, since $\Delta[\text{Benzoin}] = 2\Delta[Cu^{2+}]$, $-d[\text{Benzoin}]/dt = 2\ d[Cu^{2+}]/dt$, though, as we have shown $-d[Cu^{2+}]/dt = 2k_4[E][Cu^{+}]$.

Since it has been shown by Bartlett [3] and by Bell and Longuet-Higgins [4] that the rates of bromination of ketones and of acyloins by alkaline hypobromite measure the rates

TABLE 3. *Effect of hydroxide-ion concentration on the rate of oxidation at constant carbonate concentration.*

(Each solution contained 0·005M-copper sulphate, 0·03M-sodium citrate, 0·15M-potassium carbonate, and 0·02M-benzoin.)

Added $NaHCO_3$ (M)	pH *	$10^3[OH^-]$	$10^4 \times -d[Cu^{2+}]/dt$ (mole $l.^{-1}$ $min.^{-1}$)	$10^3 \times$ [Rate − 0·51 † $\times 10^{-4}$] / $[OH^-]$
0·00	11·91	8·13	2·35	2·26
0·01	11·66	4·57	1·23	1·58
0·02	11·45	2·82	1·05	1·91
0·03	11·30	2·00	0·89	1·90
0·04	11·19	1·55	0·80	1·87
0·05	11·13	1·35	0·79	2·07

* pH measurements were made with a Doran glass electrode and pH meter. † By extrapolation.

of their base-catalysed enolisations, this reaction has been used to find the rate of enolisation of benzoin. It has been necessary to work with very dilute aqueous solutions of benzoin since no suitable mixed solvent inert to alkaline hypobromite could be found, but fortunately the optical density of hypobromite at 331·5 mμ is sufficiently high to allow of spectrophotometric measurements being made in 10^{-3}—10^{-4}M-solution. It was found that each equivalent of benzoin reacted with two equivalents of hypobromite to give

$$Ph{\cdot}CH(OH){\cdot}COPh + 2HOBr = 2Ph{\cdot}CO_2H + 2HBr$$

benzoic acid (see Table 4), though the rate was, as expected, independent of the concentration of the hypobromite, and, with $[OBr^-]$ in large excess, a pseudo-first-order reaction (see Table 5) dependent on the alkalinity of the solution (Table 6).

TABLE 4. *Stoicheiometry of the bromination of benzoin.*

(The benzoin concentration was $2{\cdot}82 \times 10^{-4}$M.)

$[OBr^-] \times 10^4$: Initial	15·30	15·35	15·23	16·48	15·10
$[OBr^-] \times 10^4$: Final	9·7	9·95	9·89	10·96	9·40
[Benzoin]/$[OBr^-]$ reacted	1·99	1·91	1·89	1·96	2·02

TABLE 5. *Bromination of benzoin by alkaline hypobromite at 30°.*

(Initial [Benzoin], $2{\cdot}82 \times 10^{-4}$M; initial $[OH^-]$, $4{\cdot}6 \times 10^{-2}$N; initial $[OBr^-]$, $1{\cdot}52 \times 10^{-3}$M by titration.)

Time (min.)	O.D.*	$10^3[OBr^-]$ (M)	k_1 (min.$^{-1}$) (calc. from $t' = 1{\cdot}50$)	Time (min.)	O.D.*	$10^3[OBr^-]$ (M)	k_1 (min.$^{-1}$) (calc. from $t' = 1{\cdot}50$)
0	—	(1·52)	—	6·00	0·310	1·15	0·17
1·50	0·363	1·35	—	7·75	0·295	1·11	0·17
2·25	0·355	1·31	0·15	8·50	0·300	1·11	0·15
3·00	0·344	1·27	0·16	10·00	0·292	1·08	0·16
3·75	0·330	1·22	0·22	12·00	0·289	1·07	0·14
4·50	0·325	1·20	0·17	15·00	0·285	1·05	0·12
5·25	0·317	1·17	0·20	Infin.	0·267	0·98	—

Mean k_1 (graphical) = 0·177 $min.^{-1}$; $k_1/[OH^-]$ = 3·85 l. $mole^{-1}$ $min.^{-1}$.

* O.D. = Optical density.

From our measurements the velocity constant k for the oxidation of benzoin by alkaline cupric citrate at 30° has values ranging from 1·0 to 1·3 l. $mole^{-1}$ $min.^{-1}$ in the pH range 11—12, whilst that for the bromination in aqueous alkali at the same temperature is about

[3] Bartlett, *J. Amer. Chem. Soc.*, 1934, **56**, 967.
[4] Bell and Longuet-Higgins, *J.*, 1946, 636.

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3·8 l. mole^{-1} min.$^{-1}$. Both reactions obey the kinetic laws $-d[\text{Benzoin}]/dt = k[\text{Benzoin}] \times [OH^-]$ and thus the enolisation is the faster reaction by a factor of about 3.

The two reactions have perforce been measured in different solvents, but general theories of reaction kinetics in solution [5] and the directly relevant studies by Weissberger [6,7]

TABLE 6. *Rates of bromination of benzoin at different alkalinities.*

$10^2[OH^-]$ (N)	7·6	6·6	5·6	4·6	3·6
k_1 (min.$^{-1}$)	0·292	0·265	0·187	0·177	0·136
$k_1/[OH^-]$ (l. mole^{-1} min.$^{-1}$)	3·8	4·0	3·4	3·8	3·7

of the rate of autoxidation of benzoin in mixed solvents indicate that the enolisation of benzoin would probably occur even more rapidly in a solvent less polar than water. Our measurements thus give very strong support for the view that in the reactions of acyloins with cupric salts oxidation occurs much less rapidly than does enolisation.

EXPERIMENTAL

Benzoin was repeatedly crystallised from 50% acetic acid and obtained in needles, m. p. 134—135°. Dioxan, purified as described by Vogel,[8] was stored under nitrogen. Before use it was run through activated alumina to remove any traces of peroxides. A 40% (v/v) mixture with distilled water was used in kinetic experiments, a solution of benzoin in 50% dioxan being mixed with an equal volume of alkaline cupric citrate in 30% dioxan after each had been brought separately to the temperature of the thermostat. The oxidation was followed as described in Part I.[1]

Bromination of Benzoin.—Sodium hydroxide solution (approx. N), prepared from washed pellets and air-free distilled water, was standardised against potassium hydrogen phthalate. "AnalaR" bromine (0·04 ml.) was added to 20 ml. portions of this alkali and the mixtures were diluted to 100 ml. The hypobromite concentrations of these solutions were determined iodometrically, and the free hydroxide concentrations were computed by using the equation $Br_2 + 2OH^- = Br^- + OBr^- + H_2O$. Benzoin (18·7 mg.) was dissolved by shaking it in water (200 ml.), and the clear solution was diluted to 250 ml. Freshly prepared benzoin and hypobromite solutions were rapidly mixed at 30° and transferred to a 1 cm. silica cell that fitted an Adkins thermostatic cell-holder, set to 30°, inserted into a Unicam S.P. 500 spectrometer. The change in absorption of the $[OBr^-]$ ion was followed at 330 mμ wavelength by using a 0·165 mm. spectrometer slit. Under these conditions $\varepsilon_{max.}$ for $[OBr^-]$ was found to be 270. The optical density of reacting solutions decreased rapidly with time (see Table 5 for an example) but reached an almost constant value after 30—60 min. The stoicheiometry of the reaction (Table 4) was determined from the overall change of optical density. A spectroscopic test showed that the final solution contained benzoic acid and neither benzil nor benzilic acid.

One of us (B. A. M.) thanks the D.S.I.R. for a Research Studentship.

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[5] Frost and Pearson, "Kinetics and Mechanism," Chap. 7, Wiley & Sons, New York, 1953.
[6] Weissberger, Mainz, and Strasser, *Ber.*, 1929, **62**, 112.
[7] Weissberger and Bach, *J.*, 1935, 226.
[8] Vogel "Text Book of Practical Organic Chemistry," Longmans, Green & Co., London, 3rd edn. 1956, p. 177.

310. *Steroids and Walden Inversion. Part XLVII.* 5α-Cholestan-1-one, A-Nor-5α-cholestan-1-one, and Some Derivatives Thereof.*

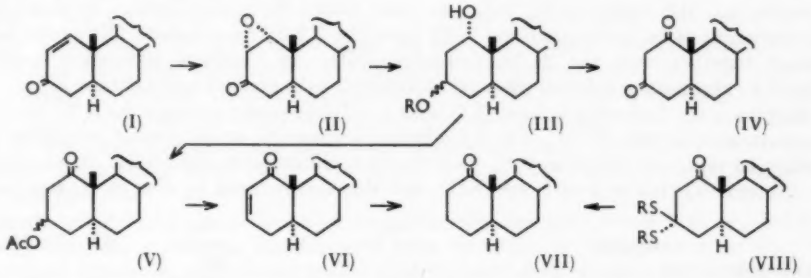
By C. W. Shoppee, S. K. Roy, and (in part) B. S. Goodrich.

5α-Cholestan-1-one has been prepared from 5α-cholest-1-en-3-one by way of 5α-cholestane-1,3-dione. Bromination of 5α-cholestan-1-one gives the 2α-bromo- and 2,2-dibromo-ketones, dehydrobrominated respectively to 5α-cholest-2-en-1-one and its 2-bromo-derivative, which may be interconverted.

1ξ-Amino-5α-cholestane, by deamination, gives 5α-cholestan-1α-ol and a mixture of 5α-cholest-1- and -2-ene; the epimeric 1-amino-5α-cholestane could not be obtained.

A-Nor-5α-cholestan-1-one has been prepared from 5α-cholest-1-ene by oxidative ring-fission to the 1,2-seco-1,2-dicarboxylic acid and pyrolysis of its barium salt; 1β-amino-A-nor-5α-cholestane, by deamination, affords A-nor-5α-cholestan-1β-ol and A-nor-5α-cholest-1-ene.

5α-Cholestan-1-one (VII) was first prepared by Striebel and Tamm [1] from 5α-cholest-1-en-3-one (I) by conversion into the 1α,2α-epoxide (II) and reduction to a mixture of 3-epimeric 5α-cholestane-1,3-diols (as III; R = H); chromatographic separation, partial acetylation at $C_{(3)}$, and oxidation of the diol 3-monoacetates (as III; R = Ac) with chromium trioxide, gave the 3-epimeric acetoxy-ketones (as V), converted by treatment with aluminium oxide into 5α-cholest-2-en-1-one (VI), hydrogenated to 5α-cholestan-1-one (VII). This ketone has also been obtained by Plattner, Fürst, and Els,[2] starting from a mixture of 5α-cholest-1- and -2-ene.



We have prepared 5α-cholestan-1-one (VII) by Striebel and Tamm's method but we found chromatographic separation of the mixture of unchanged epoxide (II), 1α,3α-diol, and 1α,3β-diol (as III; R = H) difficult and tedious; further, we were unable to achieve the essential nearly quantitative partial 3-acetylation of the 1α,3β-diol (the major product) as described by Striebel and Tamm. In an attempt to improve the preparative procedure, we examined the reaction of a synthetic 1 : 1 mixture of the epimeric diols (as III; R = H) with thionyl chloride in pyridine, whereby only the *cis*-diaxial 1α,3α-diol should yield a cyclic sulphite;[3] however, apart from chromatographically easily eluted non-crystalline material, <15% of the 1α,3β-diol could be recovered. We next investigated the oxidation of the epimeric diols, and finally found that by brief oxidation with a standard solution of chromium trioxide in sulphuric acid [4] in acetone–ether under nitrogen at 10—15° conversion

* Part XLVI, *J.*, 1960, 4874.

[1] Striebel and Tamm, *Helv. Chim. Acta*, 1954, **37**, 1094.
[2] Plattner, Fürst, and Els, *Helv. Chim. Acta*, 1954, **37**, 1399.
[3] Plattner, Segré, and Ernst, *Helv. Chim. Acta*, 1947, **30**, 1432.
[4] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.

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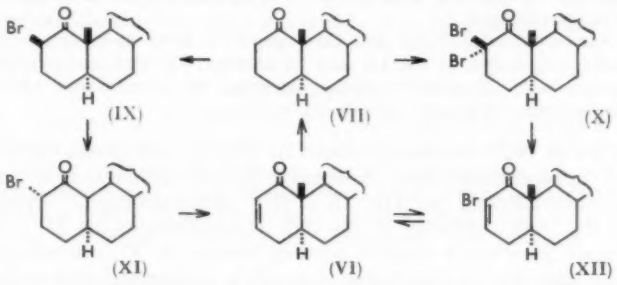
into 5α-cholestane-1,3-dione † (IV), m. p. 171°, $[\alpha]_D$ +108°, $\nu_{max.}$ 1695, 1725 cm.$^{-1}$, $\lambda_{max.}$ 256 (log ε 4·1), could be effected. The β-diketone condensed readily with toluene-ω-thiol to give the crystalline dibenzyl 3-thioketal (VIII; R = CH_2Ph), $\nu_{max.}$ 1715 cm.$^{-1}$, a process probably assisted by bonding of the 11α-hydrogen atom with the 1-carbonyl group; desulphurisation with deactivated Raney nickel[2,5] in ethanol then furnished 5α-cholestan-1-one (VII), $\nu_{max.}$ 1712 cm.$^{-1}$.

5α-Cholestan-1-one (VII), on acid-catalysed monobromination in acetic acid, gave 2α-bromo-5α-cholestan-1-one (XI), accompanied by some 2,2-dibromo-5α-cholestan-1-one (X). According to Corey,[6] the initial monobromination product should be the axial 2β-bromo-ketone (IX) (cf. ref. 7), which in the presence of hydrogen bromide passes by reduction and rebromination into the more thermodynamically stable, equatorial 2α-



bromo-ketone (XI). We attempted to obtain the 2β-bromo-ketone (IX) by base-catalysed bromination in acetic acid,[8] and by bromination in acetic acid in presence of hydrogen peroxide, but the ketone (VII) failed to react under these conditions. Acid-catalysed dibromination of 5α-cholestan-1-one (VII) gave the 2,2-dibromo-ketone (X) as the major product together with the 2α-bromo-ketone (XI); an excellent separation could be effected by chromatography on silica gel and elution with pentane and pentane–ether.

Refluxing the 2α-bromo-ketone (XI) with *s*-collidine under nitrogen for 1 hr. gave the αβ-unsaturated ketone (VI).[1] The 2,2-dibromo-ketone (X) under similar conditions was rapidly (10 min.) converted in 90% yield by ionic elimination (2βBr/3αH: *trans*, diaxial) into 2-bromo-5α-cholest-2-en-1-one (XII), and this was reduced by zinc in ethanol to the

Compound	$\nu_{max.}$ (cm.$^{-1}$)	$\Delta\nu$	$\lambda_{max.}$ (mμ)	$\Delta\lambda$	Halogen conformn.
5α-Cholestan-1-one	1712	—	297	—	
2α-Bromo-5α-cholestan-1-one	1727	+15	292 infl	−5	eq
2,2-Dibromo-5α-cholestan-1-one	1725	+13	320	+23	eq + ax
5α-Cholest-2-en-1-one	1692	—	222	—	
2-Bromo-5α-cholest-2-en-1-one	1700	+8	254	+32	—
5α-Cholestan-3-one	1718	—	286	—	
2α-Bromo-5α-cholestan-3-one	1733	+15	282	−4	eq
2,2-Dibromo-5α-cholestan-3-one	1735	+17	294	+8	eq + ax
5α-Cholest-1-en-3-one	1684	—	230	—	
2-Bromo-5α-cholest-1-en-3-one	1697	+13	256	+26	—

αβ-unsaturated ketone (VI). 2-Bromo-5α-cholest-2-en-1-one (XII) was also obtained from 5α-cholest-2-en-1-one (VI) by conversion into the crude 2,3-dibromide (cf. ref. 7) (2β,3α- and/or 2α,3β-dibromide) and passage of this through aluminium oxide.

† Since this paper was written, this dione has been reported by Tamm and Albrecht (*Helv. Chim. Acta*, 1960, **43**, 768), as also have compounds (IX), (X), (XI), and (XVIII) (m. p. 75°, [α] +11°, $\nu_{max.}$ 1727—1730 cm.$^{-1}$ in CH_2Cl_2) by Sigg and Tamm (*Helv. Chim. Acta*, 1960, **43**, 1402).

[5] Spero, McIntosh, jun., and Levin, *J. Amer. Chem. Soc.*, 1948, **70**, 1907; Rosenkranz, Kaufmann, and Romo, *ibid.*, 1949, **71**, 3689.

[6] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.

[7] Alt and Barton, *J.*, 1954, 4284.

[8] Crowne, Green, Evans, and Long, *J.*, 1956, 4354.

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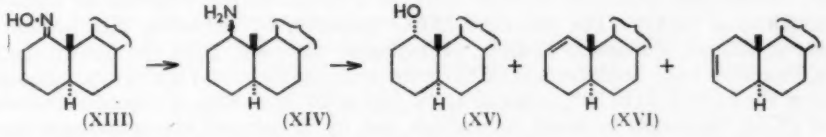
The infrared and ultraviolet spectra of 5α-cholestan-1-one and the related compounds described above support the structures assigned; they are summarised in the annexed Table, which gives for comparison the corresponding values for 5α-cholestan-3-one and related compounds.

Although optical rotatory dispersion measurements in methanol–hydrochloric acid [9] show a considerable degree of steric retardation of the 1-keto-group by the adjacent axial angular methyl group, 5α-cholestan-1-one (VII) gives a 2,4-dinitrophenylhydrazone [10] and under forcing conditions gives a single ketoxime in 75% yield. The oxime (XIII) failed to undergo the Beckmann change under a variety of experimental conditions, and, surprisingly, by reduction with sodium–alcohol, lithium aluminium hydride in ether, or hydrogen–platinum in acetic acid, gave the same 1ξ-amino-5α-cholestane (XIV), characterised as the nicely crystalline acetyl derivative. Deamination of this base (XIV) in 50% aqueous acetic acid at 20° gave 5α-cholestan-1α-ol (XV) (40%) (identified by direct comparison and by its infrared absorption spectrum; unaccompanied by 5α-cholestan-1β-ol), together with an unsaturated hydrocarbon (60%), whose infrared [11] and ultraviolet [10] absorption spectra indicated a mixture of 5α-cholest-1-ene (XVI) and the more stable 5α-cholest-2-ene.[1,2,10-12]



We have as yet been unable to prepare the 1-epimer of the base (XIV), so that the configuration of the amino-group is uncertain. It is known that rear-side α-attack is general in ring A; thus 5α-cholest-1-,[10] -2-,[13] -3-,[14] and -4-ene [15] afford α-epoxides; at $C_{(1)}$ there is additionally the steric influence of the adjacent angular β-methyl group, so that reduction of the π-component of the C=N linkage in the oxime (XIII) would be expected preferentially to furnish 1β-amino-5α-cholestane (as XIV; NH_2 equatorial). It must, however, be noted that reduction of 5α-cholestan-1-one by sodium and alcohol affords a mixture from which 5α-cholestan-1β-ol (OH equatorial) can be isolated in ~65% yield, although 5α-cholestan-1α-ol (XV; OH axial) predominates when lithium aluminium hydride is used.[1,2,10]

On the other hand, deamination of amino-steroids has been found [16] to be conformationally specific—equatorial amines react with retention of configuration to give the appropriate equatorial alcohols in nearly quantitative yield, whilst axial amines react, also with retention of configuration, to yield the appropriate axial alcohols accompanied by much unsaturated hydrocarbon. If this stereochemical pattern is carried over from positions 2, 3, 4, 6, and 7 to position 1, then deamination of the 1-amino-steroid (XIV) to give axial 5α-cholestan-1α-ol (XV) and 5α-cholest-1-ene (XVI) indicates that the base is 1α-amino-5α-cholestane (as XIV; NH_2 axial).

A-Nor-5α-cholestan-1-one (XVIII) has been prepared as follows. 5α-Cholest-1-ene (XVI), obtained from 5α-cholest-1-en-3-one (I) by reduction with lithium aluminium hydride to the 3β-alcohol, conversion of this into the 3β-chloride, and further reduction

[9] Djerassi, personal communication; cf. Djerassi, Mitscher, and Mitscher, *J. Amer. Chem. Soc.*, 1959, **81**, 947.
[10] Henbest and Wilson, *J.*, 1956, 3289.
[11] Henbest, Meakins, and Wood, *J.*, 1954, 800.
[12] Turner, Meador, and Winkler, *J. Amer. Chem. Soc.*, 1957, **79**, 4122.
[13] Fürst and Plattner, *Helv. Chim. Acta*, 1949, **32**, 275.
[14] Fürst and Scotoni, *Helv. Chim. Acta*, 1953, **36**, 1332.
[15] Shoppee, Howden, Killick, and Summers, *J.*, 1959, 630.
[16] Shoppee, Evans, and Summers, *J.*, 1957, 97; Evans and Summers, *ibid.*, p. 906; Shoppee, Cremlyn, Evans, and Summers, *ibid.*, p. 4364.

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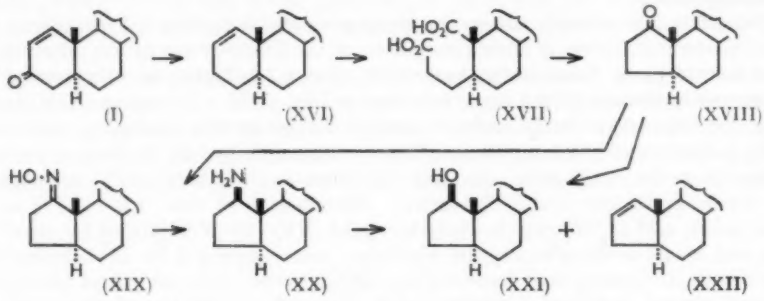
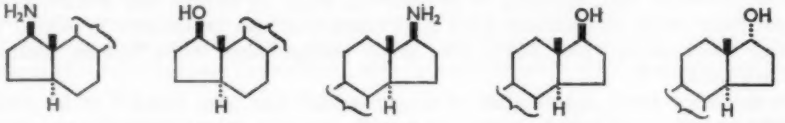
with lithium aluminium hydride,[10] was ozonised and the resulting 1,2-seco-1,2-dialdehyde oxidised to 1,2-seco-5α-cholestane-1,2-dioic acid (XVII). Pyrolysis of the barium salt yielded A-nor-5α-cholestan-1-one (XVIII), m. p. 74—76°, $[\alpha]_D$ +16°, $\nu_{max.}$ 1740 cm.$^{-1}$.



The ketone (XVIII) was reduced by sodium in alcohol, lithium aluminium hydride in ether, or hydrogen–platinum in acetic acid, to a single alcohol, regarded as A-nor-5α-cholestan-1β-ol (XXI). The ketoxime (XIX) similarly, by reduction with sodium in pentanol, lithium aluminium hydride, or hydrogen–platinum, gave the non-crystalline base, 1β-amino-A-nor-5α-cholestane (XX) characterised as the acetyl derivative. Deamination of the base (XX) in 50% aqueous acetic acid at 20° gave 80% of A-nor-5α-cholestan-1β-ol (XXI) (identified by direct comparison and by its infrared absorption spectrum), accompanied by 20% of a non-crystalline unsaturated hydrocarbon, probably A-nor-5α-cholest-1-ene (XXII).

In the absence of any other criterion, the configurations assigned to the amine (XX) and the alcohol (XXI) are based on Klyne's [17] principle of enantiomeric types. The molecular rotatory contribution of the 1-hydroxyl group in (XXI) is opposite in sign to that of the hydroxyl group in 5α-androstan-17β-ol [5,18] (as XXIV) and of like sign to that



$[M]_D$		−14°	−19°	$[M]_D$	+24°	+36°	−22°
$[M]_D$ A-nor-5α-cholestane	}	+90	+90	$[M]_D$ 5α-androstane	} +2	+2	+2
$\Delta[M]_D$		−104	−109	$\Delta[M]_D$	+22	+34	−24

of the hydroxyl group in 5α-androstan-17α-ol [18] (as XXV); similarly, the molecular rotatory contribution of the 1-amino-group in (XX) is opposite in sign to that of the amino-group in 17β-amino-5α-androstane [19] (XXIII). Approximate correspondences in magnitude are not to be expected, since the rotatory contribution of the 1-keto-group in A-nor-5α-cholestan-1-one (XVIII) is only −53° whereas that of the enantiomeric 17-keto-group in 5α-androstan-17-one is +266°.

It appears that deamination of the 1β-amine (XX) proceeds with retention of configuration accompanied by elimination. This agrees with the prediction [19] that 1β-substituted A-norsteroids should possess equatorial character in the same way as 17β-substituted steroids. It should be noted, however, that deamination of 17β-amino-5α-androstane (as

[17] Klyne, *J.*, 1952, 2916.
[18] Shoppee, *Chem. and Ind.*, 1950, 454.
[19] Shoppee and Sly, *J.*, 1959, 345.

XXIII) gives 5α-androstan-17β-ol (as XXIV) in high yield [19] unaccompanied by 5α-androst-16-ene.

Experimental

For general experimental directions see *J.*, 1959, 345. $[\alpha]_D$ refer to $CHCl_3$ solutions; ultraviolet absorption spectra were measured on a Hilger Uvispek spectrophotometer for EtOH solutions, and infrared absorption spectra on a Perkin–Elmer model 21 double-beam or on an Infracord instrument for CCl_4 solutions.

5α-Cholest-1-en-3-one (I).—2α-Bromo-5α-cholestan-3-one (m. p. 167—168°; 60 g.) was refluxed with *s*-collidine (200 ml.) in a current of dry nitrogen at 210° for 2 hr.; nitrogen was passed in for 0·5 hr. before heating and during cooling. The usual working up gave 5α-cholest-1-en-3-one (44 g., 95%), which crystallised spontaneously, and was purified by elution from aluminium oxide (1200 g.) with benzene–hexane (1 : 9 and 1 : 4; 16 × 500 ml.), and finally by recrystallisation from aqueous ethanol; it had m. p. 96—98°.

5α-Cholestane-1α,3α- and -1α,3β-diol (as III; R = H).—The above ketone (20 g.; m. p. 96—98°) by treatment with 30% hydrogen peroxide (68 ml.) and N-sodium hydroxide (200 ml.) in dioxan (800 ml.) at 20° for 20 hr. gave 1α,2α-epoxy-5α-cholestan-3-one (16 g.), m. p. 122—124° (from ethanol). The epoxide (16 g.) in ether (250 ml.) was treated with a suspension of lithium aluminium hydride (8 g.) during 30 min. After 3 hours' refluxing, isolation in the usual way gave the mixed diols (15·5 g.), which were chromatographed on aluminium oxide (500 g.) in hexane, 750 ml. portions of eluant being used. Elution with ether–benzene (1 : 9) gave fractions 1—16 containing unreduced epoxide (1·8 g.), whilst ether–benzene (1 : 4) gave fractions 17—21 consisting of epoxide and 1α,3α-diol (800 mg.); further use of ether–benzene (1 : 4) gave fractions 22—35, yielding 5α-cholestane-1α,3α-diol (4 g.) as needles, m. p. 209—211°, from ether–ethanol. Finally, use of chloroform–ether and methanol–chloroform gave fractions 36—41, affording 5α-cholestane-1α,3β-diol (8·8 g.) as prisms, m. p. 154—156°, from ethanol.

5α-Cholestane-1,3-dione (IV) [B.S.G.].—(*a*) 5α-Cholestane-1α,3α-diol (300 mg.), dissolved in acetone (50 c.c.) and a little ether, was stirred under nitrogen at 10° with a standard solution [4] of chromium trioxide in sulphuric acid (0·6 ml.). After 5 min., the green solution was diluted with water, and acetone removed at 12 mm.; extraction with ether, washing with water, drying, and evaporation gave *5α-cholestane-1,3-dione* (250 mg.) which had m. p. 174°, $[\alpha]_D$ +108° (*c*, 1·0), $\nu_{max.}$ 1695, 1725 cm.$^{-1}$, $\lambda_{max.}$ 256 mμ (log ε 4·1), after crystallisation from ether–pentane (Found: C, 81·0; H, 11·4. $C_{27}H_{44}O_2$ requires C, 80·9; H, 11·1%); it gave no colour with aqueous-alcoholic ferric chloride.

(*b*) 5α-Cholestane-1α,3β-diol (530 mg.), similarly oxidised, gave the 1,3-diketone (370 mg.), having m. p. and mixed m. p. 173° after chromatographic purification on Davison silica gel (45 g.) in hexane with elution with benzene–hexane (1 : 1).

3,3-Di(benzylthio)-5α-cholestan-1-one (VIII).—5α-Cholestane-1,3-dione (m. p. 172—174°; 110 mg.) was treated with toluene-ω-thiol (1 ml.) and 72% perchloric acid (2 drops) at 0° for 10 min. Ether-extraction and the usual working up gave *3,3-di(benzylthio)-5α-cholestan-1-one* (120 mg.), m. p. 145—147°, raised by recrystallisation from ethanol to m. p. 149—150°, $\nu_{max.}$ 1712 cm.$^{-1}$ (C=O) (Found: C, 77·8; H, 9·4. $C_{41}H_{58}OS_2$ requires C, 78·05; H, 9·7%).

5α-Cholestan-1-one (VII).—The mercaptal (VIII) (70 mg.) in ether (20 ml.) and ethanol (10 ml.) was treated with deactivated Raney nickel [3,5] at 80° for 3 hr. Filtration and evaporation of the filtrate gave a colourless oil (40 mg.), which was chromatographed on aluminium oxide (3 g.) prepared in pentane. Elution with ether–pentane (1 : 99) gave 5α-cholestan-1-one (20 mg.), m. p. and mixed m. p. 83—86°, $\nu_{max.}$ 1712 cm.$^{-1}$, after crystallisation from ether–methanol. Optical rotatory dispersion measurements, kindly made by Professor C. Djerassi, Stanford University, in methanol and methanol–hydrochloric acid at 29° show that the 1-carbonyl group is incapable of forming an acetal: $[\alpha]_{700}$ +65°, $[\alpha]_{589}$ +118°, $[\alpha]_{332}$ +388°, $[\alpha]_{317}$ +366°, $[\alpha]_{275}$ +1140° (shoulder), $[\alpha]_{250}$ +1511°, $[\alpha]_{240}$ +1780° (*c* 0·099 in methanol); and $[\alpha]_{700}$ +80°, $[\alpha]_{589}$ +112°, $[\alpha]_{332}$ +386°, $[\alpha]_{317}$ +362°, $[\alpha]_{275}$ +1115° (shoulder), $[\alpha]_{250}$ +1459°, $[\alpha]_{245}$ +1528° (*c* 0·099 in methanol–hydrochloric acid).

2α-Bromo-5α-cholestan-1-one (XI) *and 2,2-Dibromo-5α-cholestan-1-one* (X).—(*a*) 5α-Cholestan-1-one (150 mg.) in acetic acid (20 ml.) was treated with bromine (66 mg., 1·05 mol.) in acetic acid (2 ml.) and a few drops of a solution of hydrogen bromide in acetic acid at 20° for 16 hr. Water (10 ml.) was then added and after 12 hr. the crystals were collected, dried in a vacuum

(160 mg.), and chromatographed on Davison silica gel (15 g.; 100—200 mesh; W. R. Grace and Co., Baltimore, Maryland, U.S.A.) in pentane (b. p. 30—40°). Elution with ether–pentane (1 : 200; 3 × 100 ml.) gave *2,2-dibromo-5α-cholestan-1-one* (40 mg.), as needles (from chloroform–methanol), m. p. 165—167°, $[\alpha]_D$ +22° (*c* 0·65), $\nu_{max.}$ 1725 cm.$^{-1}$, $\lambda_{max.}$ 320 mμ, optical rotatory dispersion $[\alpha]_{900}$ +175°, $[\alpha]_{589}$ +221°, $[\alpha]_{345}$ −576°, $[\alpha]_{285}$ +2195°, $[\alpha]_{270}$ +1900° (*c* 0·057 in methanol at 27°) [Found (after drying at 20°/0·05 mm. for 5 hr.): C, 60·3; H, 8·15. $C_{27}H_{44}Br_2O$ requires C, 59·6; H, 8·1%]. Further elution with ether–pentane (1 : 150; 3 × 100 ml.) gave *2α-bromo-5α-cholestan-1-one* (70 mg.), plates (from chloroform–methanol), m. p. 154—156°, $[\alpha]_D$ +91° (*c* 0·8), $\nu_{max.}$ 1727 cm.$^{-1}$, $\lambda_{infl.}$ 292 mμ, optical rotatory dispersion $[\alpha]_{700}$ +79°, $[\alpha]_{589}$ +114·5°, $[\alpha]_{295}$ +726°, $[\alpha]_{265}$ +515°, $[\alpha]_{260}$ +408° (*c* 0·05 in dioxan at 25°) [Found (after drying at 20°/0·05 mm. for 5 hr.): C, 69·55; H, 9·75. $C_{27}H_{45}BrO$ requires C, 69·7; H, 9·75%]. Finally, elution with ether–pentane (1 : 200; 2 × 100 ml.) gave 5α-cholestan-1-one (20 mg.), m. p. and mixed m. p. 85·5° (from methanol).

(*b*) 5α-Cholestan-1-one (200 mg.) was similarly treated with bromine (5 mol.) in acetic acid at 20° for 5 days. The product (260 mg.) likewise was chromatographed on silica gel (30 g.) in pentane to give 2,2-dibromo-5α-cholestan-1-one (140 mg.), m. p. and mixed m. p. 165—167°, and 2α-bromo-5α-cholestan-1-one (90 mg.), m. p. and mixed m. p. 155—156°.

5α-Cholest-2-en-1-one (VI).—(*a*) 2α-Bromo-5α-cholestan-1-one (100 mg.) was refluxed with *s*-collidine (1 ml.) under nitrogen for 1 hr. The usual working up gave an oil (80 mg.), which was chromatographed on aluminium oxide (3 g.) in hexane. Elution with benzene–hexane (1 : 9) yielded 5α-cholest-2-en-1-one, having m. p. and mixed m. p. 68—69°, $[\alpha]_D$ +123° (*c* 0·8), $\nu_{max.}$ 1692 cm.$^{-1}$, $\lambda_{max.}$ 222 mμ (log ε 3·9), after crystallisation from methanol.

(*b*) 2-Bromo-5α-cholest-2-en-1-one (60 mg.) was refluxed with zinc dust in ethanol for 10 hr. Isolation of the product in the usual way and chromatography as under (*a*) gave 5α-cholest-2-en-1-one (40 mg.), m. p. and mixed m. p. 69° (from methanol).

2-Bromo-5α-cholest-2-en-1-one (XII).—2,2-Dibromo-5α-cholestan-1-one (30 mg.) was refluxed with *s*-collidine (0·5 ml.) for 10 min. under nitrogen, which was used to displace air before the reaction and during cooling of the mixture. The usual isolation procedure gave a solid (25 mg.), which by crystallisation from chloroform–methanol yielded *2-bromo-5α-cholest-2-en-1-one*, m. p. 123—125°, $[\alpha]_D$ +140° (*c*, 0·7), $\nu_{max.}$ 1700 cm.$^{-1}$, $\lambda_{max.}$ 254 mμ [Found (after drying at 15°/0·1 mm. for 5 hr.): C, 69·95; H, 9·3. $C_{27}H_{43}BrO$ requires C, 70·0; H, 9·3%].

(*b*) 5α-Cholest-2-en-1-one (100 mg.) in ether (7 ml.) was treated dropwise with bromine (41·5 mg.) in acetic acid (1 ml.) at 0°. After being left overnight, the mixture was poured into water, and the ethereal extract worked up to give crude 2,3-dibromo-5α-cholestan-1-one (130 mg.); this was dissolved in ether–pentane (1 : 9) and filtered through a column of aluminium oxide (5 g.), and the column was eluted with pentane to give 2-bromo-5α-cholest-2-en-1-one as plates (from chloroform–methanol), m. p. and mixed m. p. 123—125°, $\lambda_{max.}$ 254 mμ.

5α-Cholestan-1-one Oxime (XIII).—The ketone (2 g.) was refluxed with hydroxylamine hydrochloride (3 g.) and sodium acetate trihydrate (4 g.) in ethanol (70 ml.) for 4 hr. and isolated in the usual way. Recrystallisation from methanol gave the *oxime* (1·6 g.), m. p. 151—153° [Found (after drying at 80°/0·05 mm. for 4 hr.): C, 80·65; H, 11·1; N, 3·6. $C_{27}H_{47}NO$ requires C, 80·7; H, 11·45; N, 3·4%].

1ξ-Amino-5α-cholestane (XIV).—(*a*) The ketoxime (250 mg.) in refluxing pentanol (50 ml.) was saturated with sodium during 3 hr. After a further hour, the base was isolated by way of the ether-insoluble hydrochloride to give *1ξ-amino-5α-cholestane* as a hygroscopic oil (240 mg.), b. p. 170—180°/0·001 mm., $[\alpha]_D$ +90° (*c*, 0·6) (Found: C, 82·05; H, 12·1. $C_{27}H_{49}N,\frac{1}{2}H_2O$ requires C, 82·6; H, 12·6%), characterised as the *acetyl derivative* which had m. p. 218—220°, $[\alpha]_D$ +35° (*c*, 0·9), after recrystallisation from methanol [Found (after drying at 100°/0·05 mm. for 5 hr.): C, 80·9; H, 11·65; N, 3·25. $C_{29}H_{51}NO$ requires C, 81·05; H, 11·95; N, 3·25%]. Like the acetate of 5α-cholestan-1α-ol, which resisted prolonged heating with 3% methanolic potassium hydroxide and could only be hydrolysed by use of lithium aluminium hydride,[3] the acetyl derivative was resistant to acid and to alkaline hydrolysis.

(*b*) The ketoxime (100 mg.) in ether (30 ml.) was refluxed with an excess of lithium aluminium hydride for 4 hr. The above working up gave an oil, converted by acetic anhydride into 1ξ-acetamido-5α-cholestane, m. p. and mixed m. p. 218—220°.

(*c*) The ketoxime (100 mg.) was hydrogenated with platinum oxide (50 mg.) in acetic acid (20 ml.); after 3 hr. the base was isolated in the above way as an oil (100 mg.) converted by acetic anhydride into 1ξ-acetamido-5α-cholestane, m. p. and mixed m. p. 218—220°.

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Deamination of the Base (XIV).—1ξ-Amino-5α-cholestane (200 mg.) in a mixture of 50% acetic acid and dioxan (1 : 1) was treated dropwise with a solution of sodium nitrite (500 mg.) in 50% acetic acid, with stirring at 20°. After 24 hr. the mixture was basified with 4N-sodium hydroxide, and the product, isolated in the usual way, refluxed with 5% methanolic potassium hydroxide for 0·5 hr. The product (200 mg.) was chromatographed on aluminium oxide (6 g.) in pentane. Elution with pentane gave a hydrocarbon (120 mg.), which did not crystallise satisfactorily but gave a yellow colour with tetranitromethane in chloroform and is probably 5α-cholest-1-ene mixed with 5α-cholest-2-ene. Further elution with benzene–hexane (1 : 2) gave 5α-cholestan-1α-ol (70 mg.), alone or mixed with a genuine specimen exhibiting the double m. p. 95°/105—106°,[1] $[\alpha]_D$ +36° (*c* 0·7) (after crystallisation from methanol); its infrared absorption spectrum was identical with that of the genuine specimen.

5α-Cholest-1-ene (XVI).—5α-Cholest-1-en-3-one (m. p. 96—98°; 20 g.) was reduced with lithium aluminium hydride in ether for 3 hr. to 5α-cholest-1-en-3β-ol (17 g.), m. p. 129—131° (from ethanol); this was converted with thionyl chloride in benzene at 20° into 3β-chloro-5α-cholest-1-ene (10·5 g.), m. p. 94—100° (from acetone), which on reduction with lithium aluminium hydride in ether for 16 hr. gave, after filtration through aluminium oxide in pentane and crystallisation from acetone, 5α-cholest-1-ene (6·5 g.), m. p. 65—69°. The hydrocarbon was purified by conversion into the 1α,2β-dibromide (7 g.), m. p. 132—134° (from ethyl methyl ketone), and regeneration with zinc dust in acetic acid; extraction with pentane and filtration of the extract through aluminium oxide gave 5α-cholest-1-ene (3·6 g.), having m. p. 69—70°, $[\alpha]_D$ +13° (*c* 0·9), after recrystallisation from acetone (cf. ref. 10).

1,2-Seco-5α-cholestane-1,2-dioic Acid (XVII).—A solution of 5α-cholest-1-ene (m. p. 69—70°; 10 g.) in pure chloroform (230 ml.) was ozonised at −10° for 2 hr.; water (5 ml.) was then added and chloroform removed at 30—40°/10 mm., to afford a colourless semi-solid product. Water (5 ml.) was added and the ozonide heated to 80° during 15 min.; the mixture was dissolved in acetone (600 ml.) and oxidised with a standard solution of chromium trioxide in sulphuric acid [4] (15 ml.) at 20° overnight. After removal of chromium sulphate by filtration and of acetone under reduced pressure, the residue was taken up in ether, and 1,2-seco-5α-cholestane-1,2-dioic acid (6 g.) isolated by four-fold extraction with 2N-sodium hydroxide, acidification with 2N-hydrochloric acid, and extraction with ether as a glass, m. p. 110—130°.

A-Nor-5α-cholestan-1-one (XVIII).—The 1,2-seco-diacid (XVII) (6 g.) in 60% ethanol was neutralised with vigorous stirring by N-potassium hydroxide (phenolphthalein), and barium chloride (4 g.) in water (25 ml.) was added. The barium salt was filtered off, washed with ethanol and with ether, dried, and pyrolysed at 400—450°/1 mm. for 4 hr. The distillate (3 g.) crystallised and was purified by chromatography on aluminium oxide (150 g.) in hexane. Elution with benzene–hexane (1 : 4; 10 × 100 ml.) and recrystallisation from methanol furnished *A-nor-5α-cholestan-1-one* (1 g.) as needles, m. p. 74—76°, $[\alpha]_D$ +16° (*c* 0·9), $\nu_{max.}$ 1740 cm.$^{-1}$ [Found (after drying at 20°/0·05 mm.): C, 83·85; H, 11·9. $C_{26}H_{44}O$ requires C, 83·8; H, 11·9%].

This gave its *oxime* (XIX), m. p. 170—172° (from ethanol) [Found (after drying at 80°/0·02 mm. for 4 hr.): C, 80·3; H, 11·8; N, 3·65. $C_{26}H_{45}NO$ requires C, 80·55; H, 11·7; N, 3·85%].

A-Nor-5-α-cholestan-1β-ol (XXI).—(*a*) A-Nor-5α-cholestan-1-one (75 mg.) was hydrogenated with platinum oxide (25 mg.) in acetic acid (7 ml.) during 2·5 hr. The product, isolated in the usual manner, was an oil (80 mg.), which was chromatographed on aluminium oxide (2·5 g.) in hexane. Elution with benzene–hexane (1 : 2, 3 × 25 ml.; and 1 : 1, 4 × 25 ml.) gave *A-nor-5α-cholestan-1β-ol* (60 mg.) as prisms, double m. p. 89—91°/101—103°, $[\alpha]_D$ −5° (*c* 0·7) (after crystallisation from methanol) [Found (after drying at 60°/0·05 mm. for 4 hr.): C, 83·4; H, 12·35. $C_{26}H_{46}O$ requires C, 83·4; H, 12·35%].

(*b*) The A-nor-ketone (100 mg.) was refluxed with lithium aluminium hydride (60 mg.) in ether (25 ml.) for 2 hr. The usual isolation procedure furnished an oil (95 mg.), which by chromatography as under (*a*) gave A-nor-5α-cholestan-1β-ol (70 mg.), double m. p. and mixed double m. p. 90—91°/101—103°, $[\alpha]_D$ −5° (*c* 0·8) (after crystallisation from methanol).

1β-Amino-A-nor-5α-cholestane (XX).—The ketoxime (XIX) (200 mg.) in refluxing pentanol was saturated with sodium during 3 hr.; after a further hour, the base was isolated in the usual way and through the ether-insoluble hydrochloride, to give *1β-amino-A-nor-5α-cholestane*, b. p. 200—220°/0·15 mm., $[\alpha]_D$ −5° (*c* 0·9) (Found: C, 83·3; H, 12·4. $C_{26}H_{47}N$ requires C, 83·55; H, 12·6%), and converted with acetic anhydride into the *acetyl derivative*, m. p. 201°, $[\alpha]_D$ +33°

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(*c* 0·8) (from aqueous ethanol) [Found (after drying at 80°/0·03 mm. for 5 hr.): C, 80·8; H, 11·85. $C_{28}H_{49}NO$ requires C, 80·7; H, 11·85%].

Reduction of the ketoxime with lithium aluminium hydride in ether or its hydrogenation with platinum oxide in acetic acid gave the same 1β-amine, characterised in each case as the acetyl derivative, m. p. and mixed m. p. 201°.

Deamination of the Base (XX).—1β-Amino-A-nor-5α-cholestane (100 mg.) in a mixture of 50% acetic acid and dioxan (1 : 1) was treated dropwise with stirring with sodium nitrite (250 mg.) in 50% acetic acid overnight at 20°. After basification with 4N-sodium hydroxide, the product was extracted with ether and refluxed with 5% methanolic potassium hydroxide for 0·5 hr. Chromatography of the product (95 mg.) on aluminium oxide (3 g.) in pentane, and elution with pentane, gave a hydrocarbon, probably A-nor-5α-cholest-1-ene (20 mg.), as an oil, giving a yellow colour with tetranitromethane in chloroform. Further elution with benzene–pentane (1 : 2 and 1 : 1) yielded A-nor-5α-cholestan-1β-ol (70 mg.), double m. p. and mixed double m. p. 90°/101—103° with the specimen prepared as above, $[\alpha]_D$ −5° (*c* 0·8), whose infrared absorption spectrum was identical with that of the earlier material.

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311. *Carbohydrates of the Red Alga,* Porphyra umbilicalis.

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Extraction of the alga with hot water gives dialysable oligosaccharides and a polysaccharide fraction, the principal constituents of which are a galactan sulphate and floridean starch. The galactan sulphate, isolated by precipitation with cetylpyridinium chloride, contains D- and L-galactose, 6-*O*-methyl-D-galactose, and 3,6-anhydro-L-galactose.

The carbohydrates of red algæ (Rhodophyceæ) show a general similarity throughout the class in that they consist of (i) a water-soluble mucilage,[1] which usually contains a high proportion of a galactan, (ii) an iodophilic polysaccharide, floridean starch, which resembles glycogen or amylopectin in structure,[2] (iii) glycosides and cyclitols of low molecular weight,[3] and (iv) structural polysaccharides of the cell wall.[4] We are concerned in this paper with the carbohydrates present in the red alga *Porphyra umbilicalis* (L.) Kütz, f. *umbilicalis*, which occurs widely around the shores of Britain and is eaten in Wales under the name " laver-bread."

The dried weed, which was collected in August on the North Wales Coast, was extracted successively with cold and hot water, dilute acid, dilute alkali, and finally with hot concentrated alkali. Complete acidic hydrolysis of each extract and chromatographic examination of the sugars produced gave results essentially similar to those reported by other workers.[4,5] Since cold and hot water extracted similar material, and also since dilute acid extracted only inorganic material, extractions with cold water and with dilute acid were omitted in subsequent extractions.

More than half the dry weight of the alga was soluble in hot water and of this *ca.* 10% consisted of dialysable oligosaccharides of low molecular weight. Paper chromatography indicated that these oligosaccharides were non-reducing and that hydrolysis gave glycerol and galactose as main components, together with smaller amounts of glucose and mannose.

[1] Hirst, *Proc. Chem. Soc.*, 1958, 177; Mori, *Adv. Carbohydrate Chem.*, 1953, **8**, 315.
[2] Fleming, Hirst, and Manners, *J.*, 1956, 2831; Peat, Turvey, and Evans, *J.*, 1959, 3223, 3341.
[3] Lindberg, *Acta Chem. Scand.*, 1955, **9**, 1097.
[4] Cronshaw, Myers, and Preston, *Biochim. Biophys. Acta*, 1958, **27**, 89.
[5] Jones, *J.*, 1950, 3292.

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This is consistent with the presence in the alga of oligosaccharides of the floridoside type.[3] Floridoside and isofloridoside have since been isolated and characterised from the seaweed.[6] No oligosaccharides were present in other than the hot-water fractions. The polysaccharide fractions extracted by cold N-sodium hydroxide and by hot 20% sodium hydroxide both gave mannose, xylose, and glucose on hydrolysis, but they differed in that mannose was the main constituent from the dilute alkaline extracts while xylose was more abundant in the extracts with concentrated alkali. This is in contrast to the results obtained by previous workers.[4,5] It is apparent that mannan and xylan, together with some glucan, are the skeletal polysaccharides of this alga.

The water-soluble polysaccharides presented a complex pattern, the main constituent sugars being galactose and a sugar with the R_F value of fucose but subsequently identified as 6-*O*-methyl-D-galactose; others were glucose, mannose, arabinose, and xylose. The hydrolysate also contained degradation products of the furfuraldehyde type, later shown to be derived from 3,6-anhydro-L-galactose. No ribose or uronic acids were detected although these have been reported to be present in this alga.[4] The extract contained ester sulphate and also gave a weak red-brown stain with dilute iodine solution, indicating the presence of floridean starch. During many attempts at fractionation of this extract, galactose, 6-*O*-methylgalactose, and ester sulphate always occurred together and, therefore, presumably arise from the same polysaccharide (galactan), which also contains residues of 3,6-anhydro-L-galactose.

Fractionation of the Water-soluble Polysaccharides.—We wished to obtain specimens of the galactan and, if possible, of the floridean starch, both of which occurred in the fraction soluble in hot water. After many attempts at fractionation, the use of cationic detergents [7] as precipitants gave some success. At neutral pH, cetylpyridinium chloride precipitated the galactan component in good yield and with only traces of contaminating polysaccharides (fraction A1; see Table). When the pH of the supernatant solution was adjusted to 13,[8] a further precipitate (fraction A2) was obtained and this contained most of the floridean starch, together with some galactan and other polysaccharides. Fraction

Properties of fractions obtained from water extract of alga.

	Fraction			
	A1	A2(i)	A2(ii)	A3
Yield from fraction A (%)	53	1·2	2·4	1·0
SO_4^{2-} (%)	13·3	3·3		9·7
Iodine stain	—	—	+	—
Content of sugars (%): *				
Galactose	37·2	21·0	23·5	12·3
6-*O*-Methyl D-galactose	22·7	8·2	2·8	3·8
3,6-Anhydrogalactose	11·7		1·3	2·4
Glucose	0·2	3·7	42·0	22·0
Mannose	0·2	0·5	1·0	1·0
Xylose	0·5	1·5	1·1	6·7

* Determined after complete hydrolysis. Very small amounts of arabinose were also present in fractions A2(i) and A3.

A2 was further fractionated by using " Cetavlon " (cetyltrimethylammonium bromide) at pH 13 as precipitant: the floridean starch was not precipitated thereby [fraction A2(ii); Table] and some of the galactan impurity was removed in the precipitate [fraction A2(i); Table]. This subfractionation was not always reproducible but depended on the batch of " Cetavlon " used as precipitant. Since this detergent is a commercial preparation, it is almost certainly polydisperse with respect to alkyl chain-length. Scott [9] has

[6] Peat and Rees, *Biochem. J.*, in the press.
[7] Bera, Foster, and Stacey, *J.*, 1955, 3788; Scott, *Biochim. Biophys. Acta*, 1955, **18**, 428.
[8] Barker, Stacey, and Zweifel, *Chem. and Ind.*, 1957, 330; Palmstierna, Scott, and Gardell, *Acta Chem. Scand.*, 1957, **11**, 1792.
[9] Scott, " Methods of Biochemical Analysis," ed. Glick, Interscience Publ. Inc., New York, 1960, Vol. VIII.

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recently shown the importance of the chain-length in determining the efficiency of a cationic detergent as a precipitant for acidic polysaccharides. It is apparent that different batches of the " Cetavlon " varied somewhat in composition. A similar subfractionation of fraction A2 was, however, obtained on a small scale by electrophoresis on thick filter paper, two fractions essentially similar to A2(i) and A2(ii) being obtained.

For a detailed study of the galactan we have used fraction A1 obtained with cetylpyridinium chloride. This fraction contained N 0·3% and ash 20·5% and had $[\alpha]_D$[19] −79° (in water). It migrated as a single zone on paper electrophoresis in neutral buffer and could not be separated into further fractions by using potassium chloride as gelling agent.[10] To characterise the constituent sugars, mercaptolysis[11] was adopted. Mercaptolysis, followed by removal of thioacetal groups, gave a sugar syrup which was fractionated by chromatography on charcoal. The charcoal used was " Ultrasorb S.C. 120/240 " since this adsorbent retains monosaccharides, while salts are eluted with water, and it also gives a better separation of monosaccharides than less active charcoals.[12] Galactose, obtained from this column, was freed from traces of mannose by preparative paper chromatography. Its optical rotation and also the optical rotation of the derived galactosazone indicated a ratio of D- to L-galactose of 1 : 1·1. The 6-*O*-methyl-D-galactose crystallised and was compared with a specimen synthesized by Freudenberg and Smeykal's method.[13] From its optical rotation and that of its osazone, it is apparent that only the D-form occurs in this alga. Little 3,6-anhydro-L-galactose was obtained by this method and an alternative method of isolation was devised, based on that of Clingman *et al.*[14] Cautious hydrolysis of the polysaccharide with 0·5N-sulphuric acid resulted in scission of the 3,6-anhydrogalactosidic linkages without causing marked degradation of this sugar. Subsequent reduction with sodium borohydride and more vigorous hydrolysis then gave a mixture containing the relatively stable L-3,6-anhydrogalactitol (D-1,4-anhydrogalactitol), which was separated by column chromatography and characterised. The presence of 6-*O*-methyl-D-galactose deserves some comment since it has been reported from only a few, botanically related species of algæ, *P. capensis*,[15] *P. crispata*,[16] and *Bangia fuscopurpurea*.[17] It may well be a distinguishing feature of certain classes of alga.

Quantitative analysis of the sugars constituting the galactan gave the molar ratio galactose : 6-*O*-methyl-D-galactose : 3,6-anhydro-L-galactose : ester sulphate as 100 : 57 : 35 : 65. It is apparent, therefore, that this polysaccharide resembles that isolated from *P. capensis*[15] in the ester-sulphate content and in the component sugars. The main difference between these two polysaccharides is in the content of 3,6-anhydro-L-galactose, which appears to be lower in the *P. umbilicalis* polysaccharide.

Experimental

General Methods.—Paper chromatography and electrophoresis. The methods used for paper chromatography have been described,[18] but for the detection of sugar zones, in addition to the reagents described,[18] the *p*-anisidine hydrochloride[19] and periodate–benzidine reagents[20] were used, the former because it gives different colours with different classes of sugar and the latter for detection of glycerol and other non-reducing sugars. For the electrophoresis of polysaccharides, an acetic acid–pyridine buffer[21] was used with Whatman 3 MM. paper. Acidic

[10] Smith, Cook, and Neal, *Arch. Biochem. Biophys.*, 1954, **53**, 192.
[11] Araki and Hirase, *Bull. Chem. Soc. Japan*, 1953, **26**, 463; Percival, *Chem. and Ind.*, 1954, 1487.
[12] Hughes and Whelan, *Chem. and Ind.*, 1958, 884.
[13] Freudenberg and Smeykal, *Ber.*, 1926, **59**, 100.
[14] Clingman, Nunn, and Stephen, *J.*, 1957, 197.
[15] Nunn and von Holdt, *J.*, 1957, 1094.
[16] Jong-Ching Su, personal communication.
[17] Ya Chen Wu and Hon-Kai Ho, *J. Chinese Chem. Soc.* (*Formosa*), 1959, **6**, 84.
[18] Peat, Whelan, and Roberts, *J.*, 1957, 3916.
[19] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[20] Cifonelli and Smith, *Analyt. Chem.*, 1954, **26**, 1132.
[21] Peat, Turvey, Clancy, and Williams, *J.*, 1960, 4761.

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polysaccharides were detected with Toluidine Blue,[22] and the floridean starch with dilute iodine solution.

Hydrolysis of polysaccharides. The polysaccharide (1—20 mg.) was heated with 1·5N-sulphuric acid (0·5—2 ml.) at 100° for 3 hr., cooled, and neutralised with barium carbonate. After being filtered, the solution was concentrated at 35—40° and portions were examined by paper chromatography. If the polysaccharide was not soluble in the dilute acid, it was heated in a sealed tube with 90% formic acid (2 ml.) at 100° for 5 hr.; the cooled solution was diluted with water (10 vol.) and evaporated to dryness and the residue hydrolysed with N-sulphuric acid (5—10 ml.) at 100° for 5 hr., then neutralised and examined as above.

Analytical.—Quantitative analysis of a sugar mixture. Pridham's method [23] was used except that sugar solutions were applied to the filter paper with a modified micropipette.[24]

Estimation of 3,6-anhydrogalactose in a polysaccharide. The method, modified from that of O'Neill,[25] depends on the acidic degradation of 3,6-anhydrogalactose to 5-hydroxymethylfurfuraldehyde, which is estimated spectrophotometrically. The polysaccharide (40—100 mg.) was dissolved in water (20 ml.), 3N-hydrochloric acid (1·25 ml.) was added, and the solution diluted to 25 ml. Portions (2 ml. each) of this solution were sealed in tubes and heated at 100° for varying times (2—24 hr.). Each tube was then cooled, and the contents were washed into a 100 ml. flask containing barium carbonate (1 g.). The flasks were heated at 100° for 5 min., and water was added to 100 ml. The resulting suspension was filtered and the optical density of the filtrate measured at 285 mμ in 1 cm. cells. A curve of the logarithm of the optical density against time of heating was constructed and the later, linear portion of the curve extrapolated to zero time. From the known molar extinction coefficient of 5-hydroxymethylfurfuraldehyde (16,500) the concentration was determined.

Total sulphate. The material (50—200 mg.) was oxidised with concentrated nitric acid (20 ml.) containing sodium chloride (5—10 mg.). When the nitric acid had been evaporated off, a further 20 ml. was added and evaporated off. Last traces of nitric acid were removed by addition of concentrated hydrochloric acid and evaporation to dryness. The residue was dissolved in water and the liberated sulphate determined gravimetrically as barium sulphate.

Extraction of Seaweed.—(a) *With water.* The fresh seaweed was lightly washed with water and dried at 35° in air before being ground to a fine powder. The powder (100 g.) was stirred in water (1·5 l.) at 100° for 16 hr., and, after cooling, the residue was removed by centrifugation. This residue was then extracted as above with further portions (1·5 l. each) of water until no further material was extracted. The combined extracts were evaporated (35—40°) to 2 l. and poured slowly, with stirring, into ethanol (3 vol.). The fibrous precipitate was collected on the centrifuge, redissolved in water, dialysed against distilled water (3 × 5 l.), and reprecipitated with ethanol (3 vol.). The fibrous product (fraction A) was washed with ethanol and ether and dried over phosphoric oxide (yield 41·7 g.; ash 12·2%; SO_4^{2-}, 10·2%). After hydrolysis the following sugars were present: galactose (3+), 6-*O*-methylgalactose (3+), glucose (2+), xylose (+), mannose (+), arabinose (+), and 5-hydroxymethylfurfuraldehyde (2+).

The supernatant solution, obtained after precipitation of fraction A from the extracts, was evaporated at 35—40° to a syrup (27 g.; ash 80%), which was extracted four times with portions (100 ml. each) of boiling 85% methanol. The combined extracts were decolorised with charcoal and evaporated to a syrup (11·8 g.). A portion of this syrup was examined by paper chromatography, the periodate–benzidine spray being used to locate non-reducing sugar zones. Two main non-reducing components were detected together with traces of reducing oligosaccharides. A further portion on hydrolysis gave the following sugars: galactose (3+), glycerol (3+), glucose (+), and mannose (+).

(b) *With cold, dilute alkali.* The residue from the previous extraction was stirred at room temperature with N-sodium hydroxide (1 l.) for 16 hr. and the solids were removed by centrifugation. The solids were re-extracted repeatedly with the reagent until no further material was extracted (10 times). The combined green extracts, on acidification with hydrochloric acid (pH 3), gave a precipitate (fraction B1), which was separated, washed with alcohol to remove colouring matter, and dried as before. The residual solution was evaporated to 1 l. at 35—40° and pH 6, dialysed against tap water for 3 days, and poured into ethanol (3 vol.), to give a

[22] Ricketts, Walton, and Saddington, *Biochem. J.*, 1954, **58**, 532.
[23] Pridham, *Analyt. Chem.*, 1956, **28**, 1967.
[24] Harkins and Anderson, *J. Amer. Chem. Soc.*, 1937, **59**, 2189.
[25] O'Neill, *J. Amer. Chem. Soc.*, 1955, **77**, 2837.

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precipitate (fraction B2), which was recovered as for fraction B1. The supernatant solution contained no detectable carbohydrate. On hydrolysis fraction B1 (4·4 g.) gave mannose (3+), xylose (+), galactose (+), and glucose (trace); fraction B2 (2·0 g.) gave mannose (2+), glucose (2+), galactose (+), and xylose (trace).

(c) *With hot, concentrated alkali.* The residue from the previous extraction was stirred with 20% (w/v) sodium hydroxide (500 ml.) at 100° for 12 hr.; the solids were removed and re-extracted 3 times. The final residue (11·7 g.; ash 98%) was rejected. The extracts were acidified with hydrochloric acid to pH 3 and the precipitate formed was recovered as for previous fractions (fraction C1). The supernatant solution was dialysed until free from chloride ions, concentrated to 500 ml., and poured into ethanol (3 vol.). The precipitate was recovered as before (fraction C2). On hydrolysis, fraction C1 (5·1 g.) gave xylose (3+) and glucose (trace); fraction C2 (3·6 g.) gave xylose (2+), glucose (+), and mannose (+).

Sub-fractionation of Fraction A *with Detergents.*—Fraction A (165 g.) was stirred with water (9 l.) at 60° for 4 hr. and the residue (32 g.) then removed on the centrifuge. To the supernatant solution, cetylpyridinium chloride (120 g. per l.) was added until the precipitate just flocculated. The precipitated complex was collected on the centrifuge, the supernatant solution (X) being retained, and the precipitate was washed with 2% sodium chloride solution. The complex was redissolved by stirring overnight in 10% aqueous sodium chloride (5 l.), the insoluble residues were discarded, and the complex was reprecipitated by dialysing the solution against tap water. The complex was recovered on the centrifuge and redissolved in 10% aqueous sodium chloride (5 l.), and the polysaccharide was precipitated by the addition of ethanol (2 vol.). The precipitated polysaccharide was redissolved in water (8 l.), dialysed against tap water, and reprecipitated by addition of ethanol (3 vol.). The polysaccharide (fraction A1, Table) was washed with alcohol and ether, and dried over phosphoric oxide. To the solution (X) remaining after removal of the precipitated complex, sodium hydroxide was added to a concentration of 0·1N (pH 13) and the precipitate was collected on the centrifuge. This precipitate was washed with 0·1N-sodium hydroxide and redissolved in 10% sodium chloride solution, and the polysaccharide was recovered by pouring the mixture into ethanol (4 vol.), redissolved in water, dialysed, reprecipitated, and dried as above (fraction A2). The solution remaining after precipitation of the complex at pH 13 was neutralised and treated with potassium iodide to remove excess of detergent.[26] It was then dialysed against tap water for 2 days and poured into ethanol (3 vol.). The precipitated polysaccharides were washed and dried as above (fraction A3, Table).

Resolution of Fraction A2.—(a) *With "Cetavlon."* Fraction A2 (100 mg.) was dissolved in 0·1N-sodium hydroxide, and a solution of "Cetavlon" (B.D.H., 10 g. per 100 ml.) was added until the precipitate just flocculated. The precipitated complex was collected and dissolved in 2N-acetic acid, and the solution was poured into ethanol (4 vol.). The precipitate was redissolved, precipitated, and dried as above [fraction A2(i), Table]. The solution remaining after precipitation of the "Cetavlon" complex was neutralised, freed from "Cetavlon" by potassium iodide,[26] and dialysed against tap water. The polysaccharides were recovered from this solution by precipitation with ethanol (4 vol.), washed, and dried as above [fraction A2(ii), Table].

(b) *By paper electrophoresis.* Fraction A2 (20 mg.) was applied to Whatman 3 MM. paper and subjected to electrophoresis in neutral buffer. The paper was then dried in air and guide-strips treated with Toluidine Blue reagent to detect migrated zones of acidic polysaccharides. The remaining paper was lightly sprayed with dilute iodine solution to locate zones of floridean starch. The respective zones were cut from the paper, and polysaccharides recovered in the usual way. The sugars obtained on hydrolysis indicated that the migrating and the non-migrating (floridean starch) zone corresponded in composition to fractions A2(i) and A2(ii), respectively.

Mercaptolysis of Fraction A1.—The fraction (5 g.) was treated with hydrochloric acid and ethanethiol by O'Neill's method,[25] to give a mixture (4 g.) of sugar thioacetals. The mixture was stirred overnight at 50° with water (500 ml.) containing mercuric chloride (9 g.) and cadmium carbonate (15 g.). The mixture was then filtered and the solution saturated with hydrogen sulphide, filtered, freed from hydrogen sulphide by aeration, and neutralised with sodium hydroxide. The solution was concentrated at 30° to 100 ml. and adsorbed on a column (45 × 6 cm.) of charcoal–Celite (1 : 1, by weight), which was eluted with a linear gradient of

[26] Scott, *Chem. and Ind.*, 1955, 168.

ethanol in water (0—6% in 25 l.) and finally with 10% aqueous ethyl methyl ketone. The charcoal used was " Ultrasorb S.C. 120/240 " (British Carbo-Norit Union, Ltd.). Fractions (200 ml. each) were collected and tested for carbohydrates with the anthrone reagent.[27] The first material to be eluted was a small amount of xylose and this was followed by two major fractions containing galactose and 6-*O*-methylgalactose. The ethyl methyl ketone-eluted material giving a positive Seliwanoff reaction, but only 13 mg. of 3,6-anhydrogalactose were present.

Identification of DL-*galactose.* The galactose (0·284 g.) from the column was contaminated with a trace of mannose and it was therefore purified by chromatography on thick filter paper. The syrup obtained was dissolved in water and treated with Somogyi's deproteinising reagent,[28] and its optical rotation was measured, the concentration of galactose also being determined by Somogyi's method.[28] The value, −3·9°, obtained for the specific rotation indicated a D- to L-galactose ratio of 1 : 1·1. The galactose was characterised by conversion of a portion (140 mg.) into mucic acid, m. p. 205°, and of another portion (100 mg.) into galactosazone, m. p. 194°, $[\alpha]_D^{19}$ −5·4° (*c* 0·65 in pyridine). This value for the specific rotation of the galactosazone also indicates a D- to L-galactose ratio of 1 : 1·1.

Identification of 6-O-*methyl*-D-*galactose.* The second peak from the column was evaporated to a syrup, which contained 176 mg. of 6-*O*-methylgalactose as determined by Somogyi's method after deproteinisation.[28] The syrup was extracted with ethanol (3 × 50 ml.) and the extracts were evaporated to 20 ml. and seeded. The crystalline product had $[\alpha]_D^{18}$ +74° (final value in water), m. p. 115—116°, undepressed on admixture with 6-*O*-methyl-D-galactose synthesized by Freudenberg and Smeykal's method.[13] The osazone had $[\alpha]_D^{18}$ +137° (0 hr.) ⟶ +95° (24 hr.) in dry pyridine and m. p. 196·5—197°, mixed m. p. with authentic 6-*O*-methyl-D-galactosazone 197—197·5°.

Identification of 3,6-*Anhydro*-L-*galactose.*—Fraction A1 (18 g.) was stirred at 50° in 0·5N-sulphuric acid (2 l.) for 20 hr. and then cooled. After being neutralised with barium carbonate, the solution was filtered and evaporated to 150 ml. Sodium borohydride (2 g.) was then added and the mixture agitated gently for 16 hr., by which time only a weak Seliwanoff test was given by the solution. Excess of the borohydride was destroyed by 3N-sulphuric acid, and then sufficient acid was added to give a N-solution, which was heated at 100° for 20 hr., neutralised with barium carbonate, filtered, and evaporated to 50 ml. This solution was chromatographed on a column (120 × 5 cm.) of charcoal–Celite (B.D.H. " activated charcoal "), which was eluted with a gradient of 0—5% ethyl methyl ketone. Fractions were examined by paper chromatography and those fractions containing 3,6-anhydrogalactitol as the main constituent were bulked and evaporated to a syrup. The syrup was fractionated by chromatography on thick filter paper, 3,6-anhydro-L-galactitol being obtained as a syrup (0·57 g.), $[\alpha]_D^{19}$ −16·6° (in water). The fully benzoylated derivative[29] had m. p. 102·5—103·5°, $[\alpha]_D^{19}$ +40·5°.

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[27] Loewus, *Analyt. Chem.*, 1952, **24**, 219.
[28] Somogyi, *J. Biol. Chem.*, 1954, **160**, 61, 69.
[29] Ness, Fletcher, and Hudson, *J. Amer. Chem. Soc.*, 1951, **73**, 3742.

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312. *The Neutral Hydrolysis of Some Allyl and Benzyl Halides.*

By R. E. Robertson and J. M. W. Scott.

The rates of hydrolysis of benzyl chloride and allyl chloride, bromide, and iodide have been measured over a wide range of temperature. The derived pseudo-thermodynamic parameters for the activation process, when considered in conjunction with those derived from structurally related saturated compounds, suggest that resonance contributions to the transition state are relatively small. Evidence indicates that the transition state for these reactions in water, while being highly polar, is essentially that of a bimolecular displacement reaction.

The solvolysis of allyl and arylmethyl halides has frequently been investigated,[1-10] and more recently that of the arylmethyl halides has been used in testing aspects of theories of organic reactivity derived from the quantum theory.[2,4,11] This communication presents precise data for the hydrolysis of benzyl chloride, and allyl chloride, bromide, and iodide, representing part of a comprehensive study of the hydrolysis of simple organic halides [12] with a view to a critical examination of the current theories of nucleophilic substitution by means of the parameters $\Delta S^{\ddagger}$, $\Delta H^{\ddagger}$ and $\Delta C_p^{\ddagger}$ which characterize the activation process.

Experimental

Benzyl chloride (Eastman Kodak) was passed through alumina and fractionated twice with liberal rejection of initial and tail fractions; it had b. p. 51—52°/4 mm.; n_D^{23} 1·5374 (lit., 1·5375).

The allyl halides (Eastman Kodak) were fractionated twice with liberal rejection of initial and tail fractions; the chloride had b. p. 44·5—45°/760 mm. (lit., 44·6°), the bromide b. p. 69·5°/760 mm. (lit., 71·3°), and the iodide b. p. 98·0°/760 mm. (lit., 99·3°).

The reproducible Guggenheim plots obtained from the rate determinations [13] provided a very sensitive check as to the kinetic homogeneity of each compound. All samples were stored over silica gel, usually in the dark, especially allyl iodide which is very prone to decomposition; samples showing the colour of iodine gave solvolysis rates identical with those of freshly purified material. Samples not ultimately showing such a colour could not be prepared.

Solutions.—Solutions were prepared from the appropriate organic halide and a backing electrolyte (0·001M), which was prepared from deionized water and the potassium halide corresponding to the organic halide being studied. Before a run the appropriate weight or volume of organic halide was added to a suitable volume of backing electrolyte to give a solution (*ca.* 0·001M) which was then rapidly degassed and introduced into the conductance cells. For allyl chloride and bromide, where degassing subsequent to mixing might seriously alter the concentration of the solute, the technique was modified. A suitable quantity of organic halide was frozen in a side arm attached to a flask containing backing electrolyte which was then degassed. When degassing was complete the flask and side arm were isolated from the pumping line and the side arm was gently warmed, resulting in the solution of the organic halide.

Rate Determinations.—The rates were determined as previously described [13] in Kohlrausch conductance cells with shiny platinum electrodes. The dimensions of the cells were adjusted to give resistances of 1—30 kΩ at 1 kc. over the concentration and temperature ranges

[1] Vernon, *J.*, 1954, **243**, 4462, and references therein.
[2] Fierens and Berkowitch, *Tetrahedron*, 1957, **1**, 129, and references therein.
[3] Berliner and Shieh, *J. Amer. Chem. Soc.*, 1957, **79**, 3849.
[4] Dewar and Sampson, *J.*, 1956, 2924; 1957, 2789.
[5] Olivier, *Rec. Trav. chim.*, 1934, **53**, 891.
[6] Wilputte-Steinert and Fierens, *Bull. Soc. chim. belges*, 1956, **65**, 736.
[7] Robertson and Laughton, *Canad. J. Chem.*, in the press.
[8] Fierens and Kruys, *Bull. Soc. chim. belges*, 1956, **65**, 736; 1955, **64**, 542.
[9] Evans and Hamman, *Trans. Faraday Soc.*, 1951, **47**, 25.
[10] Bensly and Kohnstam, *J.*, 1957, 4747; 1956, 287.
[11] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341, 3345, 3350, 3353, 3355, 3357.
[12] Barnard, Heppolette, Robertson, and Scott, unpublished results.
[13] Robertson, *Canad. J. Chem.*, 1955, **33**, 1536.

investigated. Temperatures were controlled to ±0·005° and were measured with a platinum resistance thermometer in conjunction with a Leeds–Northrup 8069 Mueller bridge. The platinum resistance thermometer was calibrated by the National Research Council Heat Laboratories. The rate data so determined are recorded in Tables 1—4 together with the

TABLE 1. *Rates of hydrolysis of benzyl chloride.*

Temp.	10^5k (obs.) (sec.$^{-1}$)	10^5k (calc.) (sec.$^{-1}$)	$\Delta^\ddagger$	n	Temp.	10^5k (obs.) (sec.$^{-1}$)	10^5k (calc.) (sec.$^{-1}$)	$\Delta^\ddagger$	n
65·013°	92·71 ± 0·13	92·22	−0·0023	3	40·008°	7·659 ± 0·012	7·656	−0·00024	4
60·002	58·63 ± 0·17	58·23	−0·0030	8	35·002	4·366 ± 0·005	4·367	+0·00013	3
55·006	36·04 ± 0·07	36·15	+0·0012	6	30·011	2·437 ± 0·013	2·437	−0·0007	3
54·998	35·99 ± 0·11	36·10	+0·0013	4	20·029	0·7028 ± 0·0019	0·7031	+0·00019	4
49·988	21·96 ± 0·07	21·95	−0·0002	9	14·968	0·3562 ± 0·002	0·3592	+0·0036	3
45·001	13·12 ± 0·04	13·12	−0·00045	4					

$\Delta^\ddagger$ = log k (calc.) − log k (obs.).

TABLE 2. *Rates of hydrolysis of allyl chloride.*

Temp.	10^5k (obs. (sec.$^{-1}$)	10^5k (calc. (sec.$^{-1}$)	$\Delta^\ddagger$	n	Temp.	10^5k (obs.) (sec.$^{-1}$)	10^5k (calc.) (sec.$^{-1}$)	$\Delta^\ddagger$	n
84·990°	68·41 ± 0·23	68·30	−0·00071	3	65·006°	11·48 ± 0·02	11·49	+0·00062	8
82·467	55·45 ± 0·30	55·37	−0·00062	4	60·036	7·050 ± 0·012	7·045	−0·00029	4
80·023	44·96 ± 0·06	45·03	+0·00069	3	54·996	4·194 ± 0·008	4·230	+0·0037	4
77·497	36·03 ± 0·065	36·19	+0·0018	4	50·024	2·473 ± 0·005	2·470	−0·00028	4
74·990	29·08 ± 0·11	29·02	−0·00098	4	40·002	0·7908 ± 0·0021	0·7893	−0·00083	4
69·919	18·32 ± 0·02	18·30	−0·00050	4	34·997	0·4294 ± 0·0017	0·4300	+0·00063	3

TABLE 3. *Rates of hydrolysis of allyl bromide.*

Temp.	10^5k (obs.) (sec.$^{-1}$)	10^5k (calc.) (sec.$^{-1}$)	$\Delta^\ddagger$	n	Temp.	10^5k (obs.) (sec.$^{-1}$)	10^5k (calc.) (sec.$^{-1}$)	$\Delta^\ddagger$	n
65·007°	142·3 ± 0·2	141·8	−0·0015	6	39·955°	10·77 ± 0·01	10·74	−0·0011	4
59·999	88·96 ± 0·43	88·51	−0·0022	4	35·063	6·057 ± 0·009	6·054	−0·0002	4
54·983	54·21 ± 0·07	54·06	−0·0012	4	30·052	3·268 ± 0·009	3·269	+0·0001	4
51·006	36·13 ± 0·09	35·97	−0·0019	4	25·005	1·698 ± 0·005	1·712	+0·0035	4
50·886	35·63 ± 0·05	35·52	−0·0013	3	20·036	0·8710 ± 0·001	0·8768	+0·0029	3
50·002	32·39 ± 0·07	32·40	+0·0015	4	14·997	0·4294 ± 0·001	0·4312	+0·0018	3
44·987	18·88 ± 0·06	18·90	+0·0005	4					

TABLE 4. *Rates of hydrolysis of allyl iodide.*

Temp.	10^5k (obs.) (sec.$^{-1}$)	10^5k (calc.) (sec.$^{-1}$)	$\Delta^\ddagger$	n	Temp.	10^5k (obs.) (sec.$^{-1}$)	10^5k (calc.) (sec.$^{-1}$)	$\Delta^\ddagger$	n
75·013°	129·7* ± 0·7	124·5	—	3	55·037°	16·61 ± 0·05	16·62	+0·0002	6
72·449	100·0* ± 0·2	97·82	—	6	49·995	9·541 ± 0·012	9·525	−0·0007	4
70·011	78·02 ± 0·24	77·47	−0·0031	4	45·025	5·381 ± 0·011	5·366	−0·0012	6
67·595	60·61 ± 0·12	61·18	+0·0040	6	40·023	2·924 ± 0·012	2·937	+0·0019	8
64·994	46·84 ± 0·13	47·26	+0·0038	6	29·986	0·8668 ± 0·0065	0·8108	+0·0021	4
63·483	36·80 ± 0·07	36·62	−0·0021	8	24·967	0·4103 ± 0·0012	0·4086	−0·0018	6
59·992	28·56 ± 0·065	28·29	−0·0041	8					

* Not used in computing A, B, and C by least-squares method for reasons given on p. 1598.

TABLE 5. *Constants and derived parameters from the three-parameter equation* (1) *for benzyl chloride and allyl chloride, bromide, and iodide.*

	Benzyl chloride	Allyl chloride	Allyl bromide	Allyl iodide
A	−7306·022	−8345·295	−8794·772	−8304·459
B	−19·30920	−24·18912	−28·72687	−22·55956
C	67·40443	81·91612	95·81302	78·28866
$\Delta C_p^\ddagger$	−40·4	−50·1	−59·1	−46·7
$\Delta H_0^\ddagger$	33·430	38·185	40·242	37·999
$\Delta S_0^\ddagger$	220·85	277·47	332·12	264·32

$\Delta C_p^\ddagger$ in cal. mole^{-1} deg.$^{-1}$; $\Delta H_0^\ddagger$ in kcal. mole^{-1}; $\Delta S_0^\ddagger$ in cal. mole^{-1} deg.$^{-1}$.

root-mean-square deviation from n separate first-order plots. The temperature dependence of the rates could be expressed within the experimental error by the equation

$$\log k = A/T + B \log T + C \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

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The values of A, B, and C for each individual compound were determined by the method of least squares. By adopting the usual convention,[14]

$$A = -\Delta H_0^{\ddagger}/2{\cdot}3026\boldsymbol{R} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$B = \Delta C_p^{\ddagger}/\boldsymbol{R} + 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$C = (\Delta S_0^{\ddagger} - \Delta C_p^{\ddagger})/2{\cdot}3026\boldsymbol{R} + \log \boldsymbol{k}/\boldsymbol{h} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $$\Delta H_T^{\ddagger} = \Delta H_0^{\ddagger} + \Delta C_p^{\ddagger} T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and $$\Delta S_T^{\ddagger} = \Delta S_0^{\ddagger} + 2{\cdot}3026\Delta C_p^{\ddagger} \log T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

we converted empirical quantities A, B, and C into the pseudo-thermodynamic parameters $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta C_p^{\ddagger}$. Values of A, B, and C appropriate to each compound are recorded in

FIG. 1. *Allyl chloride* ▽, *allyl bromide* □, *allyl iodide* ●, *benzyl chloride* ○.

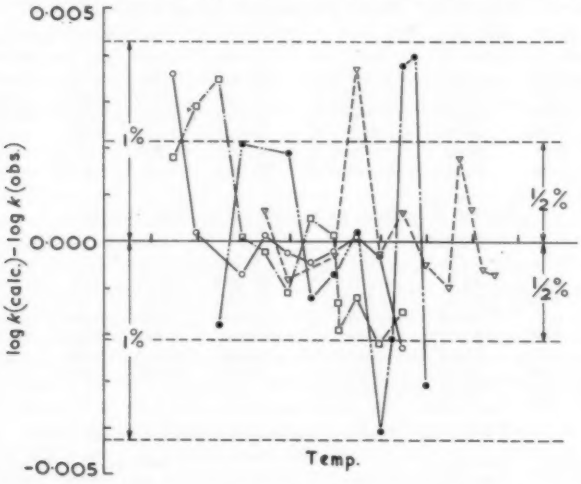

Table 5 together with the derived values of $\Delta H_0^{\ddagger}$, $\Delta S_0^{\ddagger}$, and $\Delta C_p^{\ddagger}$. Values of $\Delta H_T^{\ddagger}$ and $\Delta S_T^{\ddagger}$ at 0°, 25°, 50°, and 100° are recorded in Table 6.

TABLE 6. *Enthalpies and entropies of activation for benzyl chloride and allyl chloride, bromide, and iodide at various temperatures.*

	Benzyl chloride		Allyl chloride		Allyl bromide		Allyl iodide	
Temp.	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
0·00°	22·41	−5·56	24·51	−3·34	24·11	0·73	25·25	2·51
25·00	21·40	−9·09	23·26	−7·73	22·63	−4·46	24·08	−1·58
50·00	20·39	−12·34	22·01	−11·76	21·15	−9·20	22·91	−5·34
75·00	19·38	−15·35	20·76	−15·49	19·68	−13·61	21·74	−8·82
100·00	18·37	−18·15	19·51	−18·96	18·20	−17·71	20·58	−12·05

$\Delta S^{\ddagger}$ is in cal. mole^{-1} deg.$^{-1}$. $\Delta H^{\ddagger}$ is in kcal. mole^{-1}.

Errors and Previous Results.—In Fig. 1 the function log k (calc.) − log k (obs.) is plotted against temperature. The deviations are quite random and are usually $<\frac{1}{2}\%$ except for allyl iodide where they are somewhat greater. Allyl iodide was the most difficult to investigate for reasons which are not completely understood. At the end of some of the determinations the reaction solutions were coloured, and the colour was proved to be due to free iodine. Such coloration was especially prevalent in the high-temperature region and was perhaps due to the incursion of some free-radical process.

Robertson, *J. Chem. Phys.*, 1956, **25**, 375.

TABLE 7. *Previously reported results for the hydrolysis of benzyl chloride.*

Temp.	Ref.	k (obs.) (sec.$^{-1}$)	k (calc.) * (sec.$^{-1}$)	Temp.	Ref.	k (obs.) (sec.$^{-1}$)	k (calc.) * (sec.$^{-1}$)
30°	5	$2{\cdot}42 \times 10^{-5}$	$2{\cdot}43 \times 10^{-5}$	40·00°	6	$7{\cdot}76 \times 10^{-5}$	$7{\cdot}66 \times 10^{-5}$
25	2	$1{\cdot}38 \times 10^{-5}$	$1{\cdot}32 \times 10^{-5}$	47·10	6	$1{\cdot}61 \times 10^{-4}$	$1{\cdot}63 \times 10^{-4}$
20·02	6	$7{\cdot}65 \times 10^{-6}$	$7{\cdot}31 \times 10^{-6}$	60·000	7	$5{\cdot}828 \times 10^{-4}$	$5{\cdot}823 \times 10^{-4}$
30·00	6	$2{\cdot}51 \times 10^{-5}$	$2{\cdot}43 \times 10^{-5}$				

* Calculated from the above three-parameter equation: so also in Tables 8 and 9.

TABLE 8. *Previously reported results for the hydrolysis of allyl chloride.*

Temp.	Ref.	k (obs.) (sec.$^{-1}$)	k (calc.) * (sec.$^{-1}$)	Temp.	Ref.	k (obs.) (sec.$^{-1}$)	k (calc.) * (sec.$^{-1}$)
19·10°	8	$5{\cdot}36 \times 10^{-7}$	$5{\cdot}22 \times 10^{-7}$	50·00°	8	$2{\cdot}62 \times 10^{-5}$	$2{\cdot}46 \times 10^{-5}$
25·00	8	$1{\cdot}11 \times 10^{-6}$	$1{\cdot}18 \times 10^{-6}$			$2{\cdot}74 \times 10^{-5}$	
40·00	8	$8{\cdot}34 \times 10^{-6}$	$7{\cdot}89 \times 10^{-6}$	74·989	7	$2{\cdot}948 \times 10^{-4}$	$2{\cdot}90 \times 10^{-4}$

TABLE 9. *Previously reported results for the hydrolysis of allyl bromide.*

Temp.	Ref.	k (obs.) (sec.$^{-1}$)	k (calc.) (sec.$^{-1}$)	Temp.	Ref.	k (obs.) (sec.$^{-1}$)	k (calc. (sec.$^{-1}$)
15·00°	8	$4{\cdot}21 \times 10^{-6}$	$4{\cdot}32 \times 10^{-6}$	51·00°	8	$3{\cdot}47 \times 10^{-4}$	$3{\cdot}60 \times 10^{-4}$
25·00	8	$1{\cdot}62 \times 10^{-5}$	$1{\cdot}71 \times 10^{-5}$	60·00	7	$8{\cdot}94 \times 10^{-4}$	$8{\cdot}85 \times 10^{-4}$
40·00	8	$1{\cdot}06 \times 10^{-4}$	$1{\cdot}08 \times 10^{-4}$				

In Tables 7—9 previous results for the rates of hydrolysis of benzyl chloride, allyl chloride, and allyl bromide in water are recorded [k (obs.)], together with rates calculated [k (calc.)] from the appropriate three-parameter equation. These results are in satisfactory agreement with our own.

DISCUSSION

The method of proceeding from the parameters $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta C_p^{\ddagger}$ to conclusions regarding the properties of the transition state is not clear. Winstein [15] has noted that these parameters do not provide a sufficient basis for the systematization of the effect of structure on reactivity, without allied initial-state data. A similar viewpoint has been adopted by Moelwyn-Hughes [16] and a detailed discussion made by Robertson, Heppolette, and Scott.[17] Evans and Hamman [9] noted a parallelism between the entropy of ionization for amines and the entropy of activation for structurally related solvolytic substrates, *e.g.*, trimethylamine and t-butyl chloride, etc. These relationships were considered to demonstrate the similarity in solvation between ammonium and carbonium ions. Kohnstam [10] has suggested that the ratio $\Delta C_p^{\ddagger}/\Delta S^{\ddagger}$ can be used as diagnostic of mechanism but the basis of this test has not been clearly stated. By using the method adopted in this communication for converting A, B, and C of equation (1) into $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta C_p^{\ddagger}$, Kohnstam's ratio becomes

$$\Delta C_p^{\ddagger}/\Delta S^{\ddagger} = \Delta C_p^{\ddagger}/(\Delta S_0^{\ddagger} + \Delta C_p^{\ddagger} \ln T) \quad . \quad . \quad . \quad . \quad . \quad (7)$$

For all the substrates [12] where the parameters $\Delta S_0^{\ddagger}$ and $\Delta C_p^{\ddagger}$ have been determined, the former has always been positive and the latter negative. In consequence, the denominator of equation (7) will become zero when $T = \exp(-\Delta S_0^{\ddagger}/\Delta C_p^{\ddagger})$ and the ratio infinite. Below this temperature $\Delta S^{\ddagger}$ is positive and above it negative, so as well as displaying a discontinuity the ratio will also change sign. Two of the compounds reported in this paper behave in this way between 0° and 100°, as do several others for which data are available.[7] It is difficult to envisage the physical significance of a ratio which behaves in this manner. The fact that the entropy of activation changes sign within the range of experimental investigation also makes the sign and magnitude of this quantity difficult to interpret. In consequence, the most satisfactory way of using the available entropy

[15] Winstein and Fainburg, *J. Amer. Chem. Soc.*, 1957, **79**, 5937.
[16] Moelwyn-Hughes, *Proc. Roy. Soc.*, 1952, *A*, **220**, 386.
[17] Robertson, Heppolette, and Scott, *Canad. J. Chem.*, 1959, **37**, 803.

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data appears to be to discuss changes in $\Delta S^{\ddagger}$ with variations in the structure of the substrate.*

Heat Capacities of Activation.—The heat capacities of activation for the four organic halides now reported are all negative, in conformity with previous studies in water, alcohol, and mixed solvents.[10,13,17] These heat-capacity changes are of the same sign and magnitude as those derived from studies of the ionization of weak acids.[18] The latter is an unambiguous ionogenic reaction and in consequence the heat capacity is in the present study suggestive of an ionization. These heat capacities of activation do not show the

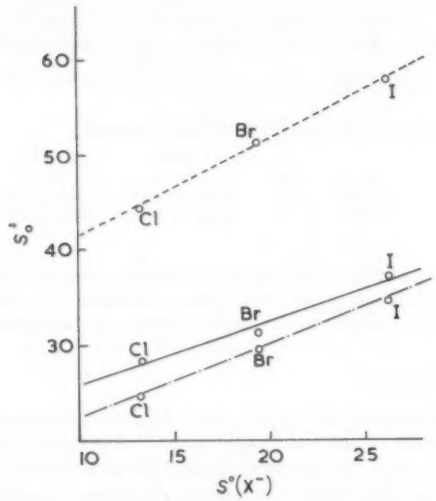


FIG. 2.
. . . . s-Pr; —— Me; —·—·— Allyl.
Temp. 298·16°.

same kind of relation as are found between the free energy, enthalpy, and entropy of activation for the methyl and allyl series (see below). This parameter, however, is obtained from the second differential of the rate with respect to temperature and so is the least accurate of the derived parameters. Alternatively, the heat capacities of activation may reflect finer differences in the activation process to which the free energy and enthalpy are insensitive.

Entropy of Activation.—It was noted on p. 1599 that the pseudo-thermodynamic parameters which characterize the activation process do not provide a sufficient basis for the discussions of differences in transition states of solution reactions. Robertson, Heppolette, and Scott [17] have suggested that the equation

$$S^0_{\ddagger} = S_g^0 + \delta_s S + \Delta S^{\ddagger} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

can be used to characterize the transition state. Unfortunately, in the present instance only $\Delta S^{\ddagger}$ of the terms on the right-hand side of equation (8) is known and hence some means

* This is part of a wider problem presented by the data which are reported. The quantities $\Delta H_s^{\ddagger}$ and $\Delta S_s^{\ddagger}$ probably have no significance but are artifacts arising from the convention used for converting A, B, and C of our empirical equation (1) into pseudo-thermodynamic parameters. A similar situation arises with the parameters obtained from studies of the dissociation constants of weak acids over a wide temperature range (cf. Everett and Wynne-Jones [18]). However, the quantities $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ at any temperature between 0° and 100° are considered to have significance. The temperature dependence of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ is a consequence of heat-capacity terms (see below and Table 6) and requires the choice of some arbitrary temperature for their comparison. For water this is logically 50°, although this will not always coincide with the temperature of optimum accuracy of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for individual substrates, which is the middle point of experimental range over which the temperature dependence of the rate is determined.

[18] Everett and Wynne-Jones, *Trans. Faraday Soc.*, 1939, **35**, 1380.

of estimating S_g^0 and $\delta_g S$ are necessary. The initial-state data for the methyl halides where S_g^0 and $\delta_g S$ are known, can be used for the allyl halides.[12] $S_\ddagger^0$ for the methyl and the s-propyl halides is linearly related to the standard-state entropy S^0 (X^-) of the corresponding halide ion: see ref. (17) and Fig. 2.

$$S_\ddagger^0 = mS^0(X^-) + c \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

A similar relation holds for the allyl chloride, bromide, and iodide, the value of m being intermediate between that found for the methyl and the s-propyl halides. Superficially, the value of m could be considered to indicate the charge development in the transition state,[17] but such a direct interpretation of the variation of m with the nature of the organic group needs further consideration.

The standard-state entropy of a monatomic ion can be divided into three parts, and

FIG. 3.

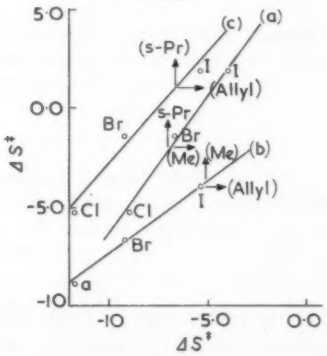
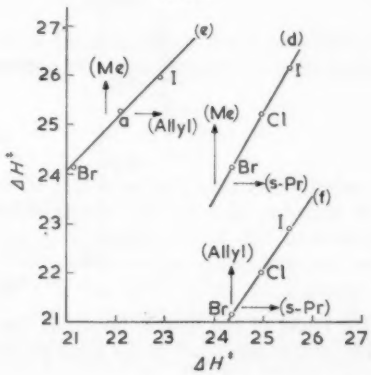


FIG. 4.



several equations have been suggested for this purpose. For reasons which have been stated elsewhere,[17] the equation due to Laidler [19] will be adopted:

$$S^0(X^-) = \tfrac{3}{2}R \ln M - Aq^2e^2/r_u + \text{const.} \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where q is the charge and e is the electronic charge, A a constant, and r_u the univalent radius of the ion.

The first two terms in equation (10) represent respectively the translational and electrostatic entropy (Born charging) of the ions. If in equation (9) m is equal to unity, this suggests that the ions are completely formed in the transition state, since they must have their full complement of solvating water molecules and also their full ionic translational entropy. However, values of $m < 1$ do not immediately imply that the charge development is less than unity, *i.e.*, the charge development could be unity but the translational entropy might be less than that appropriate to free ions. Whilst the evidence presented here gives little detailed information of what is occurring around the group R (which is part of the molecule where mechanistic questions are important) it does suggest that the positive charge on the organic part must approach unity in the transition state, irrespective of how it is distributed. The entropies of activation as might be expected from equation (9) also give relationships of the form (see Figs. 3 and 4 and Table 11):

$$\Delta S^\ddagger(A) = m\Delta S^\ddagger(B) + \text{const.} \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

and similarly for the enthalpy of activation:

$$\Delta H^\ddagger(A) = m'\Delta H^\ddagger(B) + \text{const.}' \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

[19] Laidler, *Canad. J. Chem.*, 1956, **34**, 1107.

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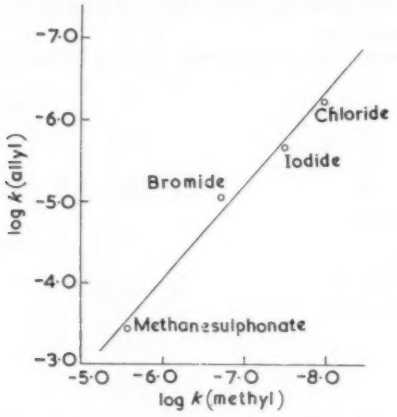
where *e.g.*, A = Me and B = Allyl, etc. It is tentatively suggested that these relationships indicate a common mechanistic pattern.

Resonance Contributions to the Transition State: The Free Energy and Enthalpy of Activation.—The benzyl and allyl halides all react faster than the corresponding methyl and ethyl * compounds in water. The increase in rate in both cases is due solely to a decrease in the enthalpy of activation since the corresponding entropy trends are $\Delta S^{\ddagger}(\text{Me}) \sim \Delta S^{\ddagger}(\text{Et}) > \Delta S^{\ddagger}(\text{Allyl}) > \Delta S^{\ddagger}(\text{Benzyl})$ (Tables 10 and 6). The reasons for this negative trend in entropy with increasing unsaturation are not clear but may originate

FIG. 5.



from the effect of the double bonds on the solvation of the initial state.[7] Allyl chloride, bromide, and iodide react in the same peculiar [7] rate sequence as the corresponding methyl

TABLE 10. *Enthalpies and entropies of activation for the methyl and ethyl halides at* 50·00°.

	Chloride		Bromide		Iodide	
	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
Methyl	25·26	−8·89	24·14	−6·65	25·95	−3·94
Ethyl	24·96	−5·24	24·26	−7·10	25·61	−3·61

For sources of these data and methods of calculation see refs. 12 and 17.

TABLE 11. *Thermodynamic and related data for equations* (11) *and* (12).

$T = 50{\cdot}00°$

Entropy equation (see Fig. 3)

A	B	*m*	const.	Curve
s-Pr	Me	1·38	7·41	*a*
Allyl	Me	1·26	−0·543	*b*
s-Pr	Allyl	1·13	8·27	*c*

Observed and values calculated from the curves

	s-Pr obs.	s-Pr calc. from *a*	s-Pr calc. from *c*	Allyl calc. from *b*	
Cl	−5·25	−4·98	−4·98	−11·76	−11·85
Br	−1·43	−1·79	−2·09	−9·20	−8·93
I	1·86	1·96	2·25	−5·34	−5·51

Enthalpy equation (see Fig. 4)

A	B	*m′*	const.′	Curve
s-Pr	Me	0·632	9·07	*d*
Allyl	Me	0·935	−1·91	*e*
s-Pr	Allyl	0·695	10·44	*f*

Observed and values calculated from the curves

	s-Pr obs.	s-Pr calc. from *d*	s-Pr calc. from *f*	Allyl calc. from *e*	
Cl	24·96	25·04	24·93	22·01	22·16
Br	24·36	24·32	24·37	21·15	21·10
I	25·52	25·47	25·53	22·91	22·81

* The ethyl halides are probably best considered as the primitive member of the above series but since they have not been investigated kinetically over as wide a range of temperature as the methyl halides the latter will be used for some of the comparisons.

halides: Br > I > Cl. The approximate linear free-energy relationships between the allyl and methyl derivatives again suggest a common mechanism (see Table 12 and Fig. 5).

The enhancement of reactivity of allyl and benzyl solvolytic substrates over that shown by structurally related saturated compounds is usually attributed to an increase in resonance energy in proceeding from the reactants to the transition state.[1,20] Resonance

TABLE 12. *Rate data for the methyl and allyl series: T = 20·02°.*

	k (allyl) (sec.$^{-1}$)	k (methyl) (sec.$^{-1}$)		k (allyl) (sec.$^{-1}$)	k (methyl) (sec.$^{-1}$)
Chloride ...	$5{\cdot}94 \times 10^{-7}$	$1{\cdot}07 \times 10^{-8}$ 12	Iodide	$2{\cdot}02 \times 10^{-6}$	$3{\cdot}32 \times 10^{-8}$ (12)
Bromide ...	$8{\cdot}74 \times 10^{-6}$	$1{\cdot}76 \times 10^{-7}$ 12	Methanesulphonate	$3{\cdot}61 \times 10^{-4}$ (12)	$2{\cdot}70 \times 10^{-6}$ (12)

energy is a potential energy and is correctly discussed in terms of ΔE_0 of the absolute rate equation:

$$k = (kT/h)Z^{\ddagger}Z \exp(-\Delta E_0/RT) \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

where ΔE^0 is the difference in the zero-point levels of the reactants and the transition state. Unfortunately, the enthalpy of activation measured at room temperatures is indirectly related to ΔE^0:

$$\Delta H^{\ddagger} = \Delta E^0 + \int_0^T C_p^{\ddagger} \,.\, \mathrm{d}T - \int_0^T C_p \,.\, \mathrm{d}T = \Delta E^0 + \int_0^T \Delta C_p^{\ddagger} \,.\, \mathrm{d}T$$

At temperatures for which the data are reported, $\Delta C_p^{\ddagger}$ is large and negative but even with this added information conclusions are not possible about ΔE^0 since in principle $\Delta C_p^{\ddagger}$ is also a function of temperature. Evans and Polanyi [21] suggested that $\Delta G^{\ddagger}$ behaves more like ΔE^0 than does $\Delta H^{\ddagger}$ and in consequence potential-energy quantities are usually discussed in terms of the free-energy parameter.[1,4] Our $\Delta H^{\ddagger}$ values at a given temperature do follow the expected trends in ΔE^0, with increased unsaturation in the side chain. Hence, the decrease in the energy of activation in the allyl and benzyl compounds can be tentatively attributed to increased resonance, from the reactants to the transition state.

It does not appear possible to give a consistent interpretation of electronic effects for a given reaction if the transition states are changing in character. The methyl, ethyl, allyl, and benzyl halides are generally considered to react at different positions along the S_N1–S_N2 spectrum,[21,23] and indeed the values of m in equation (9), where they have been determined, indicate that something of this nature is occurring. In the gas phase, the methyl, ethyl, allyl, and benzyl carbonium ions show very considerable differences in stability as shown in the variation of the enthalpy of the reaction [23] $RX \longrightarrow R^+ + X^-$, and these differences, although still apparent in the solvolytic reaction, are considerably reduced. The entropy relationship, equation (9), is compatible with complete charge transfer in the transition state but the enthalpies of activation (Tables 10 and 6) imply that if the positive charge is stabilized internally then some factor is responsible for the reduction in the differences which are apparent in the gaseous ionization. This is obviously the solvation of the positive charge (cf. Mason [23]).

Our discussion suggests that the transition states for the solvolytic reaction in water can be either (I) or (II), where (I) involves only non-specific interaction with the positive charge (S_N1) and (II) involves definite covalent interaction (S_N2) as well as non-specific solvation. There is some evidence to suggest that in water (II) is the more probable. Winstein and Marshall [24] have pointed out that, in the methyl, ethyl, s-propyl, and t-butyl

[20] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N.Y., 1953, Ch. 6, and references therein.
[21] Polanyi and Evans, *Trans. Faraday Soc.*, 1936, **32**, 1333.
[22] Streitwieser, *Chem. Rev.*, 1956, **56**, 571.
[23] Mason, *J.*, 1958, 808.
[24] Winstein and Marshall, *J. Amer. Chem. Soc.*, 1952, **74**, 1120.

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halides, the addition of each methyl group should be equivalent to a factor of six units in log k if the reaction is limiting in character. In water the s-Pr : Me ratios are small,[12] from which, on the basis of the above premise, it is concluded that for primary and secondary centres these reactions are not limiting in character. Also the benzyl : allyl

(I) (II)

ratios at 25° for the reactions (*a*) bimolecular I–Cl exchange in acetone, (*b*) hydrolysis, and (*c*) formolysis are respectively: 2·2,[25,26] 11·0, and 45.[9] Thus even if limiting kinetics (S_N1) is assumed in formic acid, which is very dubious for primary centres,[22,27] we must conclude that the reaction is not limiting (S_N1) in character in water, and takes place by what is essentially a bimolecular displacement reaction in which the transition state is very polar.

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[*Received, February 22nd,* 1960.]

[25] Fierens, *Bull. Soc. chim. belges*, 1959, **68**, 177.
[26] Fierens, *Helv. Chim. Acta*, 1955, **37**, 2009.
[27] Streitwieser, *J. Amer. Chem. Soc.*, 1955, **77**, 1117.

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313. *Poly-*p*-xylylene and Related Polymers.*

By J. H. Golden.

Poly-*p*-xylylene and some related polymers have been prepared in good yields by the reaction of phenyl-lithium with di(halogenomethyl) aromatic compounds.

Although poly-*p*-xylylene has been extensively investigated on account of its high thermal stability, most of the work was done with polymers prepared by the pyrolysis of *p*-xylene. Such polymers are sparingly soluble in organic solvents, owing [1,2] to slight cross-linking of the essentially linear chains, and other syntheses [3,4] lead to more readily soluble products. The pyrolytic method is available [5] for the preparation of related polymers, but potential starting materials must be thermally stable and are restricted to those aromatic compounds containing two methyl groups *para* to each other. Accordingly, the formation of polymers by the coupling of di(bromomethyl) compounds, a less severe method of wider potential applicability, has been investigated. Coupling of *p*-di(bromomethyl)benzene by magnesium,[6] Grignard reagents,[7] or sodium [2,3,6,8] yields poly-*p*-xylylene and, since bromomethylarenes are readily coupled [9] by phenyl-lithium (*e.g.*, as in the preparation of aceanthrene,[10] acenaphthene,[11] and 2,3:6,7-dibenzophenanthrene,[12] etc.), the preparation of polymers by this route has been studied.

Reaction of *p*-xylylene dibromide with phenyl-lithium gave poly-*p*-xylylene (74%). Infrared examination of this material, and of specimens prepared by Wurtz–Fittig condensation of the dibromide with sodium–potassium alloy and by pyrolysis of *p*-xylene, revealed

[1] Corley, Haas, Kane, and Livingston, *J. Polymer Sci.*, 1954, **13**, 137.
[2] Auspos, Burnam, Hall, Hubbard, Kirk, Schaefgen, and Speck, *J. Polymer Sci.*, 1955, **15**, 19.
[3] Vansheydt, Mel'nikova, Kukhareva, and Krakovyak, *Zhur. priklad. Khim.*, 1958, **31**, 1898.
[4] Schaefgen, *J. Polymer Sci.*, 1959, **41**, 133; du Pont de Nemours, B.P. 807,196.
[5] Errede and Swarc, *Quart. Rev.*, 1958, **12**, 302.
[6] Jacobson, *J. Amer. Chem. Soc.*, 1932, **54**, 1513.
[7] Carothers, *Chem. Rev.*, 1931, **8**, 353.
[8] Brown and Farthing, *J.*, 1953, 3270; Muller and Roscheisen, *Chem. Ber.*, 1957, **90**, 543.
[9] Wittig and Witt, *Ber.*, 1941, **74**, 1474.
[10] Bergmann and Ikan, *J. Org. Chem.*, 1958, **23**, 907.
[11] Bergmann and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1953, **75**, 2760.
[12] Bergmann and Ikan, *J. Amer. Chem. Soc.*, 1958, **80**, 208.

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their identity, except that slight carbonyl absorption (1681 cm.$^{-1}$) was present only in the pyrolysis product. *X*-Ray powder photographs showed that the phenyl-lithium product was in the α-lin. form described by Brown and Farthing.[8] The molecular weight (M_N 8200) of the phenyl-lithium polymer was calculated from the bromine content, by assuming all end-groups to be bromine; this method is not completely reliable as the presence of some hydrogen end-groups is probable. The polymer was appreciably soluble in high-boiling aromatic solvents.

Poly-*p*-xylylene was also prepared by treating *p*-xylylene dibromide with lithium, but in lower yield, and the product had a lower softening point and smaller molecular weight than the product from the phenyl-lithium reaction.

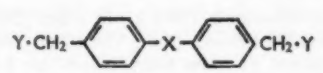
Poly(tetramethyl-*p*-phenylenedimethylene), similarly prepared from *p*-di(chloromethyl)-durene by Wurtz–Fittig reaction and by the action of phenyl-lithium on *p*-di(-iodomethyl)-durene was not appreciably soluble in organic solvents and softened above 400°.

Poly-(2,5-dimethoxy-1,4-phenylenedimethylene) was obtained by reaction of phenyl-lithium with 1,4-di(-iodomethyl)-2,5-dimethoxybenzene. The low softening point (238°) and ease of solubility in bromoform and aromatic solvents of this polymer, as compared with poly-*p*-xylylene, suggests that the substituent methoxy-groups have an internal plasticising effect. The dimethoxy-polymer readily underwent Zeisel cleavage to the corresponding dihydroxy-polymer but attempted oxidation of this by chromic oxide to the poly-quinone was unsuccessful.

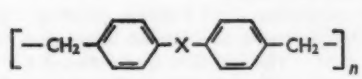
The preparation of the di(halogenomethyl) compounds (I; Y = Cl, Br, and I) and their reaction with phenyl-lithium to give the polymers (II) was undertaken since these polymers are inaccessible by the pyrolytic route.

The ether (Ia; Y = H) with bromine in the presence of ultraviolet light gave a complex mixture from which a small quantity of di-*p*-(bromomethyl)phenyl ether was isolated; however, reaction with *N*-bromosuccinimide (cf. selective bromination of methyl-naphthalenes [13]) yielded the required product in good yield. The sulphone (Ib; Y = H) was brominated by *N*-bromosuccinimide (with difficulty) and by bromine,[14] both products after extensive fractional crystallisation yielding di-*p*-(bromomethyl)phenyl sulphone. The ketone (Ic; Y = Br) was also prepared by using *N*-bromosuccinimide, but difficulties were again encountered in the purification. The presence of polyhalogenomethyl contaminants among the products of both the bromine [14] and the *N*-bromo-succinimide [15] reaction is probable.

The iodomethyl compounds (Ia, b, c; Y = I) prepared by halogen exchange from the bromomethyl compounds (Ia, b, c; Y = Br), and di(iodomethyl)durene all showed a



(Ia) X=O ; (Ib) X=SO$_2$
(Ic) X=CO



(IIa) X=O ; (IIb) X=SO$_2$
(IIc) X=CO

marked tendency to lose iodine and correct analytical figures were difficult to obtain. The acetoxy-compounds (Ia, b, c; Y = OAc) were prepared by the action of silver acetate on the bromo-compounds. The 4,4′-di(acetoxymethyl)benzophenone, m. p. 79°, was homogeneous and casts doubt on the purity of the 4,4′-di(chloromethyl)benzophenone prepared by Connerade [16] which, on treatment with silver acetate, yielded a mixture of oil and crystals, m. p. 42—48°, described as the acetoxy-compound (Ic; Y = OAc).

Treatment of the sulphone (Ib; Y = H) with sulphuryl chloride yielded the

[13] Doukas, *J. Chem. Educ.*, 1954, **31**, 12; Ried and Bodem, *Chem. Ber.*, 1958, **91**, 1981.
[14] Horner and Medem, *Chem. Ber.*, 1952, **85**, 520.
[15] Horner and Winkelmann, *Angew. Chem.*, 1959, **71**, 356.
[16] Connerade, *Bull. Soc. chim. belges*, 1933, **42**, 311.

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chloro-compound (Ib; Y = Cl), but similar reactions with the ether and ketone yielded complex mixtures which could not be completely separated.

The polymers (IIa, b) were prepared by the action of phenyl-lithium on the bromo-compounds (Ia, b; Y = Br). The poly-ether, softening point 185°, was readily soluble in halogenated solvents and aromatic hydrocarbons; its molecular weight was determined by end-group analysis (5070) and cryoscopy (6300). The poly-sulphone was almost insoluble in organic solvents and had a much higher softening point [>360° (decomp.)].

The product obtained by reaction of a mixture of *p*-xylylene dibromide and di-*p*-(bromomethyl)phenyl ether with phenyl-lithium gave elemental analyses and an infrared spectrum between those of the two homopolymers. The low solubility and high melting point suggest a copolymer rather than a mixture of two homopolymers, one of which should be readily extractable.

Treatment of 4,4′-di(bromomethyl)benzophenone with phenyl-lithium did not yield polymer, as a preferred reaction involved the carbonyl group; the microanalysis and infrared analysis of the product were consistent with the structure 4,4′-di(bromomethyl)-triphenylmethanol.

The infrared spectra of all the polymers prepared by phenyl-lithium reactions closely resembled those of the respective simple dimethyl compounds, apart from the aliphatic vibrations, and this, together with the other physical properties examined, suggests an essentially linear structure for these polymers.

The ether (Ia; Y = H) was oxidised to the corresponding di-acid which was converted (cf. Conix [17]) into its poly-anhydride, softening point 315—320°, sparingly soluble in high-boiling aromatic solvents.

The reported reaction [18] of 4-bromobenzyl bromide with butyl-lithium to give 4-*p*-bromobenzylbenzyl bromide, m. p. 112—113°, was re-investigated, as extension of this reaction would provide a route to the unknown poly-*p*-benzylene:

$$Br{\cdot}C_6H_4{\cdot}CH_2Br \longrightarrow Br{\cdot}C_6H_4{\cdot}CH_2{\cdot}C_6H_4{\cdot}CH_2Br \longrightarrow [C_6H_4{\cdot}CH_2]_n$$

In the present case only 1-bromo-4-pentylbenzene (24%) and 4,4′-dibromobibenzyl (49%), m. p. 114—116°, were isolated. It appears that the reported [18] compound of m. p. 112—113° was in fact the bibenzyl so that the reaction is analogous to the coupling of *o*-bromobenzyl bromide.[19]

Experimental

Yields of polymers are based on the theoretical structures, end-groups etc. being neglected. Softening points given for polymers are the temperatures at which viscous melts were obtained on a Kofler hot-stage.

Poly-p-xylylene.—(a) *Lithium coupling.* *p*-Xylylene dibromide (26·4 g.) in ether (200 ml.) was added dropwise to a stirred suspension of finely divided lithium (5·6 g.) in ether (100 ml.) during 1 hr. The solution was refluxed for 24 hr., stirred at room temperature for 3 days, treated with methanol (100 ml.), and poured into 5% acetic acid (1 l.). Filtration yielded a solid (7·2 g.) which was exhaustively extracted with ether, leaving a white powder (6·7 g., 64%). Extraction of a sample with 4 : 1 ethanol–concentrated hydrochloric acid and organic solvents gave poly-*p*-xylylene [Found: C, 89·2; H, 7·7; Br, 2·9. Calc. for $(C_8H_8)_{51}Br_2$: C, 89·7; H, 7·4; Br, 2·9%], softening pt. 230—233°, soluble in high-boiling solvents, *e.g.*, nitrobenzene, biphenyl, diphenyl ether.

(b) *Phenyl-lithium coupling.* An ether solution of phenyl-lithium (7·64 g. in 250 ml.) was added dropwise to a stirred solution of *p*-xylylene dibromide (24 g.) in ether (400 ml.) during 45 min. The white suspension was refluxed for 30 min. and then decomposed with 10% acetic acid (200 ml.). After filtration and separation *p*-xylylene dibromide (2·3 g.) was recovered from the ether layer. The white precipitate was extracted (Soxhlet) with ether, leaving poly-*p*-xylylene (6·3 g., 74%), almost insoluble in high-boiling solvents. Extraction of a sample as in (a) caused no loss in weight. The polymer [Found: C, 90·7; H, 7·5; Br, 1·95. Calc. for

[17] Conix, *Makromol. Chem.*, 1957, **24**, 76; *J. Polymer Sci.*, 1958, **29**, 343.
[18] Rosenberg, *J. Amer. Chem. Soc.*, 1954, **76**, 4389.
[19] Letsinger and Skoog, *J. Amer. Chem. Soc.*, 1955, **77**, 5176.

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$(C_8H_8)_{77}Br_2$: C, 90·4; H, 7·6; Br, 2·0%] had a softening pt. >370° and *X*-ray powder pattern: 5·38s, 4·00s, 3·50vw, 3·06vw, 2·81vw Å (compare α-lin form [8]).

Di(chloromethyl)durene.—Hydrogen chloride was passed into a stirred mixture of durene (100 g.), paraformaldehyde (92 g.), and anhydrous zinc chloride (200 g.) in glacial acetic acid (2 l.) at 70—80° during 24 hr. The cooled solution was filtered from grey crystals (122 g.), m. p. 185°, and the liquors were treated with water to yield a second crop of crystals. Recrystallisation of the combined crops from benzene gave di(chloromethyl)durene (112 g., 65%), m. p. 196° (Rhoad and Flory [20] give m. p. 193—194°).

Di(iodomethyl)durene.—Sodium iodide (80 g.) in acetone (200 ml.) was added to a solution of di(chloromethyl)durene (46 g.) in refluxing acetone. After refluxing for 4 hr. the mixture was poured into water (4 l.). The washed precipitate (78·5 g.), m. p. 213° (decomp.), recrystallised from chloroform as pale yellow needles (70 g., 85%), m. p. 213° (decomp.). Further recrystallisation (from benzene) gave pure *di(iodomethyl)durene* (Found: C, 35·1; H, 3·8; I, 61·6. $C_{12}H_{16}I_2$ requires C, 34·8; H, 3·9; I, 61·3%), m. p. 214° (decomp.).

*Poly(tetramethyl-*p*-phenylenedimethylene)*.—(a) *Coupling by sodium–potassium alloy*. Sodium–potassium alloy (1·5 g.) was added dropwise to a stirred solution of di(chloromethyl)-durene (5 g.) in dioxan (125 ml.) at 60° during 1 hr. The temperature was raised during 1 hr. and the solution then refluxed for 10 hr. Ethanol–light petroleum (b. p. 60—80°) (1 : 10) was added and the sludge filtered off, washed with ethanol and water, and dried. The *polymer* [Found: C, 87·5, 88·3; H, 9·1, 9·6; Cl, 0·34, 0·33. $(C_{12}H_{16})_n$ requires C, 90·0; H, 10·0%] (2·7 g., 78%) was obtained as a cream powder softening at >400°, having negligible solubility in organic solvents. The combined liquors were treated with benzene and water; the benzene layer yielded a cream solid (1 g.), softening pt. 165—180°. (b) *Phenyl-lithium coupling*. Phenyl-lithium (10·3 g.) in ether (250 ml.) was added to a refluxing solution of di(iodomethyl)-durene (25·3 g.) in benzene (500 ml.) during 1·5 hr., the ether being removed by distillation. The solution was refluxed for a further 1 hr., kept overnight, decomposed with methanol (50 ml.), and poured into 10% hydrochloric acid (1 l.). The white solid was filtered off, washed thoroughly, dried, and then refluxed with ethanol–concentrated hydrochloric acid (1 : 1). The washed, dried *polymer* [Found: C, 86·5; H, 9·3; I, 4·3. $(C_{12}H_{16})_{35}I_2$ requires C, 86·0; H, 9·6; I, 4·3%] (9·6 g., 98%) had softening pt. >400°. The polymer was almost insoluble in high-boiling solvents but was swollen by 1-chloronaphthalene and benzyl benzoate. The *X*-ray powder pattern was 5·72m, 4·07w, 3·87w, 3·29vw Å.

2,5-*Di(iodomethyl)*-1,4-*dimethoxybenzene*.—2,5-Di(chloromethyl)-1,4-dimethoxybenzene [21] underwent halogen exchange with sodium iodide in acetone, to give 2,5-*di(iodomethyl)*-1,4-*dimethoxybenzene* (96%), as pale yellow needles (from acetone or benzene) (Found: C, 28·5; H, 3·3; I, 61·0. $C_{10}H_{12}I_2O_2$ requires C, 28·7; H, 2·9; I, 60·7%), decomp. 136°. The iodo-compound lost iodine when heated alone or in, *e.g.*, toluene.

Poly-(2,5-*dimethoxy-*p-*phenylenedimethylene*).—Phenyl-lithium (8·4 g.) in ether (250 ml.) was added to a stirred refluxing solution of 2,5-di(iodomethyl)-1,4-dimethoxybenzene (20·9 g.) in benzene (300 ml.) during 1 hr., the ether being removed continuously. After a further hour the brown reaction mixture was decomposed with water (500 ml.), just acidified, and filtered. The precipitated polymer was washed with methanol and water and dried (7·1 g.). The product was purified by precipitation from bromoform into methanol, refluxed with ethanol–concentrated hydrochloric acid (1 : 1) for 8 hr., washed with water and ethanol, and dried (6·6 g., 80%). *Poly-*(2,5-*dimethoxy-*p-*phenylenedimethylene*) [Found: C, 73·0; H, 7·6; I, 2·6. $(C_{10}H_{12}O_2)_n$ requires C, 73·15; H, 7·3%] was obtained as a white powder, softening pt. 238°, soluble in bromoform and aromatic solvents.

Poly- (2,5-*dihydroxy-* p-*phenylenedimethylene*).—Poly-(2,5-dimethoxy-*p*-phenylenedimethylene) [Found: MeO, 34·5. $(C_{10}H_{12}O_2)_n$ requires MeO, 37·8%] underwent Zeisel cleavage to give the infusible 2,5-*dihydroxy-polymer* [Found: C, 71·0; H, 5·2; I, 2·9. $(C_8H_8O_2)_n$ requires C, 70·6; H, 5·9%] as a chocolate-brown powder, insoluble in organic solvents and aqueous potassium hydroxide.

*Di-*p-*(bromomethyl)phenyl Ether*.—(a) *Use of* N-*bromosuccinimide*. A mixture of *N*-bromosuccinimide (80 g.) and benzoyl peroxide (1 g.) was added in portions during 20 min. to a refluxing solution of di-*p*-tolyl ether [22] (40 g.) and benzoyl peroxide (0·5 g.) in benzene (120 ml.). The

[20] Rhoad and Flory, *J. Amer. Chem. Soc.*, 1950, **72**, 2216.
[21] Shimizu and Maki, *J. Pharm. Soc. Japan*, 1951, **71**, 958.
[22] Barrett, Drumm, and Reilly, *J.*, 1927, 67.

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cooled solution was filtered from succinimide (44·4 g.; m. p. 127°), washed with aqueous sodium hydroxide and water, dried (Na_2SO_4; charcoal), filtered, and concentrated. The solid residue (75·2 g.), recrystallised from cyclohexanol, had m. p. 92° (43·9 g., 61%). Extractive recrystallisation from light petroleum (b. p. 60—80°) yielded the *dibromo-ether* (Found: C, 47·3; H, 3·7; Br, 44·9. $C_{14}H_{12}Br_2O$ requires C, 47·2; H, 3·4; Br, 44·9%) as colourless flakes, m. p. 98°.

(b) *Use of bromine.* Di-*p*-tolyl ether (19·8 g.) at 200—220° was irradiated with ultraviolet light and treated dropwise with bromine (32 g.) during 30 min. Working up yielded a neutral oil (44·2 g.) which on distillation (accompanied by considerable decomposition) yielded a fraction (4·1 g.), b. p. 231—240°/0·5 mm., n_D^{22} 1·6192, m. p. 87° alone or mixed with material prepared as under (a).

(c) *Reduction.* Di-*p*-(bromomethyl)phenyl ether (0·76 g.) and zinc dust (3 g.), suspended in acetic acid (20 ml.), were treated with a few drops of aqueous cupric sulphate and refluxed for 6 hr. Working up of the product gave di-*p*-tolyl ether (0·35 g.), m. p. and mixed m. p. 48—49° (from light petroleum).

(d) *Hydrolysis.* Di-*p*-(bromomethyl)phenyl ether (10 g.) was refluxed with 15% aqueous potassium hydroxide (100 ml.) for 32 hr. Working up yielded a glassy *diphenol* (6·2 g.) (Found: C, 77·3; H, 5·7%. $H{\cdot}[C_{14}H_{12}O_2]_3{\cdot}OH$ requires C, 77·0; H, 5·85%), m. p. 87—88°, soluble in aromatic hydrocarbons, dioxan, and chloroform, insoluble in light petroleum, alcohols, and esters.

Di-p-(*bromomethyl*)*phenyl Sulphone.*—(a) *Use of bromine.* Di-*p*-tolyl sulphone [23] (85 g.) at 160—180° was irradiated with ultraviolet light and treated dropwise with bromine (35·4 ml.) during 1 hr. After a further 2 hr. at 160° the mixture was poured into chloroform (1 l.) and was washed with aqueous sodium carbonate and water and dried (Na_2SO_4; charcoal). The filtrate was evaporated. The residue (140 g.), m. p. 90—95°, was fractionally crystallised (8 stages) from methanol–chloroform and benzene–cyclohexane alternately, yielding colourless plates of di-*p*-(bromomethyl)phenyl sulphone (Found: C, 41·6; H, 3·0; Br, 40·0; S, 8·35. Calc. for $C_{14}H_{12}Br_2O_2S$: C, 41·6; H, 3·0; Br, 39·55; S, 7·9%), m. p. 148—149° (Horner and Medem [14] give m. p. 148°). Di-*p*-tolyl sulphone was recovered after being refluxed for 6 hr. with bromine in carbon tetrachloride under ultraviolet irradiation. (b) *Use of* N-*bromosuccinimide.* A solution of di-*p*-tolyl sulphone (41 g.), *N*-bromosuccinimide (69 g.), and benzoyl peroxide (1·5 g.) in carbon tetrachloride (120 ml.) was refluxed for 32 hr. Working up as described for the ether gave a brown oil (63 g.) which on extensive fractional crystallisation, as in (a), yielded the dibromo-sulphone (2·5 g.), m. p. 143—146°. No reaction occurred when di-*p*-tolyl sulphone was treated with *N*-bromosuccinimide under the conditions described for the corresponding ether.

4,4′-*Dimethylbenzophenone.*—Condensation of toluene and carbon tetrachloride was carried out according to Gomberg and Todd's directions,[24] but distillation of the crude oily product led to polymerisation. However, addition of light petroleum (b. p. 40—60°) to the oil at 0° yielded the ketone which, recrystallised from light petroleum (b. p. 60—80°), had m. p. 90—91° (30% yield).

4,4′-*Di*(*bromomethyl*)*benzophenone.*—Di-*p*-tolyl ketone (84 g.) with *N*-bromosuccinimide (160 g., 10% excess) gave a product (194 g.) that, crystallised by extraction (Soxhlet) with cyclohexane, had m. p. 120—123° (65 g.). This was difficult to purify but extensive fractional crystallisation from chloroform–ethanol and cyclohexane yielded needles (12 g.) of 4,4′-*di*-(*bromomethyl*)*benzophenone* (Found: C, 48·9; H, 3·1; Br, 43·8. $C_{15}H_{12}Br_2O$ requires C, 49·0; H, 3·3; Br, 43·4%), m. p. 138—139°.

Di-p-(*iodomethyl*)*phenyl Ether.*—A solution of di-*p*-(bromomethyl)phenyl ether (5 g.) and sodium iodide (10 g.) in acetone (200 ml.) was refluxed for 1 hr. and poured into water (1·5 l.). Filtration gave a pale yellow solid (5·5 g., 88%), m. p. 104—105°. Recrystallisation from acetone–methanol and light petroleum (b. p. 60—80°) yielded *di*-p-(*iodomethyl*)*phenyl ether* (Found: C, 37·75; H, 2·8; I, 56·45. $C_{14}H_{12}I_2O$ requires C, 37·4; H, 2·7; I, 56·4%) as pale yellow needles, m. p. 107—108°.

Di-p-(*iodomethyl*)*phenyl Sulphone.*—Di-*p*-(bromomethyl)phenyl sulphone was converted, as was the corresponding ether, into the *iodo-compound* (90%), needles (from methanol–acetone and chloroform–light petroleum) (Found: C, 34·2; H, 2·5; I, 50·4; S, 6·4. $C_{14}H_{12}I_2O_2S$ requires C, 33·8; H, 2·4; I, 51·0; S, 6·4%), m. p. 169°.

4,4′-*Di*-p-(*iodomethyl*)*benzophenone.*—The dibromo-ketone was converted, as was the ether,

[23] Meyer, *Annalen*, 1923, **433**, 327.

into the *iodo-compound* (95%, yellow needles (from acetone–methanol and cyclohexane) (Found: C, 39·4; H, 2·8; I, 54·3. $C_{15}H_{12}I_2O$ requires C, 39·0; H, 2·6; I, 54·9%), m. p. 141°.

Di-p-(*acetoxymethyl*)*phenyl Ether*.—Di-*p*-(bromomethyl)phenyl ether (3 g.) in acetic acid (50 ml.) at 75° was treated with a solution from silver oxide (4 g.) in acetic acid (25 ml.). The mixture was refluxed for 15 min., cooled, and filtered (kieselguhr) from silver bromide into water (1·5 l.). Extraction with ether and working up of the extract gave a sticky solid (2·3 g.), m. p. 44°, very soluble in organic solvents. Recrystallisation from light petroleum (b. p. 30—40°) yielded *di*-p-(*acetoxymethyl*)*phenyl ether* (Found: C, 68·8; H, 6·0. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%) as colourless leaflets, m. p. 50°. The acetoxy-compound was not obtained by the action of lead tetra-acetate on di-*p*-tolyl ether in acetic acid.

Di-p-(*acetoxymethyl*)*phenyl Sulphone*.—Di-*p*-(bromomethyl)phenyl sulphone was converted, as described for the ether, into the *acetoxy-compound* (83%) needles from benzene–light petroleum (b. p. 60—80°) (Found: C, 59·4; H, 5·1; S, 9·15. $C_{18}H_{18}O_6S$ requires C, 59·65; H, 5·0; S, 8·8%, m. p. 107°.

4,4′-*Di*-p-(*acetoxymethyl*)*benzophenone*.—Di-*p*-(bromomethyl)benzophenone was converted, as described for the ether, into the acetoxy-compound (96%), needles from light petroleum (b. p. 40—60°) (Found: C, 70·1; H, 5·2. Calc. for $C_{19}H_{18}O_5$: C, 69·9; H, 5·6%), m. p. 79° (Connerade [16] gives m. p. 42—48°).

Di-p-(*chloromethyl*)*phenyl Sulphone*.—Benzoyl peroxide (0·75 g.) and sulphuryl chloride (18 ml.) in carbon tetrachloride (40 ml.) were added to a refluxing solution of di-*p*-tolyl sulphone (24·6 g.) and benzoyl peroxide (0·25 g.) in carbon tetrachloride (150 ml.) during 1 hr. The mixture was refluxed for a further 16 hr., cooled, diluted to 500 ml. with carbon tetrachloride, washed with aqueous sodium hydrogen carbonate and water, dried (K_2CO_3), filtered, and concentrated to an oil (32·4 g.). When diluted with cyclohexane and kept for several weeks at 0° this afforded a solid (7·6 g.), m. p. 114—118°, whence recrystallisation from light petroleum (b. p. 60—80°) (yield 6·2 g.) and then from methanol gave *di*-p-(*chloromethyl*)*phenyl sulphone* (Found: C, 55·0; H, 3·85; Cl, 22·9; S, 10·4. $C_{14}H_{12}Cl_2O_2S$ requires C, 53·35; H, 3·8; Cl, 22·5; S, 10·2%) as colourless rods, m. p. 139°. Treatment of this compound with sodium iodide in acetone gave the iodo-compound, m. p. and mixed m. p. 169°. No halogen interchange occurred on treatment of the chloro-compound with sodium or potassium bromide in acetone.

Reaction of Di-p-tolyl Ether with Sulphuryl Chloride.—Chlorination of the ether (19·8 g.), as described for the sulphone, gave an oil which on repeated distillation yielded a fraction (0·89 g.), b. p. 233—234°/17 mm., n_D^{24} 1·5942 (Found: C, 61·8; H, 4·8; Cl, 27·2. Calc. for $C_{14}H_{12}Cl_2O$: C, 62·9; H, 4·5; Cl, 26·5%), which partly crystallised (m. p. 59°) (Plieninger, Horn, and Lutz [25] give m. p. 68°).

Reaction of 4,4′-*Dimethylbenzophenone with Sulphuryl Chloride*.—Chlorination of the ketone (21 g.), as described for the sulphone, gave a sticky solid (32·5 g.), recrystallisation of which from cyclohexane and light petroleum yielded needles (16·8 g.), m. p. 103° (Found: C, 64·7; H, 4·4; Cl, 25·25. Calc. for $C_{15}H_{12}Cl_2O$: C, 64·5; H, 4·3; Cl, 25·4%). Connerade [16] gives m. p. 110·5° for di-*p*-(chloromethyl)phenyl ketone. Attempted conversion of the chloro- into the acetoxy-derivative yielded an intractable mixture.

Poly-[p,p′-*oxidodi*(*phenylmethylene*)] (IIa).—(a) *Homopolymer*. Phenyl-lithium (9·44 g.) in ether (250 ml.) was added dropwise to a stirred solution of di-*p*-(bromomethyl)phenyl ether (20 g.) in ether–benzene (500 ml.; 10 : 1) during 1 hr. The solution was stirred for a further 15 min., decomposed with water (200 ml.), and filtered. The white precipitate was washed with 2N-hydrochloric acid, water, and ethanol, and dried (9·9 g.). Addition of a filtered benzene solution of the solid to ether, and repetition of this procedure, yielded the *poly-oxide* [Found: C, 82·9; H, 6·1; Br, 3·2%; *M*, cryoscopic in naphthalene, 6300. $(C_{14}H_{12}O)_{25}Br_2$ requires C, 82·95; H, 6·0; Br, 3·15%; *M*, 5066] as a white powder (6·9 g., 63%), softening pt. 185° The polymer was soluble in aromatic hydrocarbons, chloroform, and bromoform, but insoluble in acids, alcohols, and light petroleum, and swollen by cyclohexanol and carbon tetrachloride. On *X*-ray powder analysis it gave lines at 4·68s, 4·37w, 4·27m, 4·14s, 3·26m Å, and it had $\nu_{max.}$ 1241s, 1259s (aromatic ether), 2855, 2920 cm.$^{-1}$ (CH stretch). Di-*p*-tolyl ether had $\nu_{max.}$ 1242s, 2859, 2872, 2919 cm.$^{-1}$.

(b) *Copolymer with poly*-(p-*phenylenedimethylene*). A refluxing solution of di-*p*-(bromomethyl)phenyl ether (18 g., 1·1 mol.) and *p*-xylylene dibromide (12·35 g., 1 mol.) in benzene

[24] Gomberg and Todd, *J. Amer. Chem. Soc.*, 1917, **39**, 2392.
[25] Plieninger, Horn, and Lutz, *Arch. Pharm.*, 1953, **286**, 285.

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(350 ml.) was treated dropwise with phenyl-lithium (4·32 g.) in ether (140 ml.) during 45 min., ether being removed throughout. After a further 15 min. the mixture was worked up as in (a), to yield a white powder (5·7 g.) which closely resembled poly-*p*-xylylene in solubility. Extraction with alcohols and ether left the *copolymer* (5·6 g.) (Found: C, 86·2; H, 7·1; Br, 5·6%. Analysis intermediate between those of the homopolymers), m. p. >400°, $\nu_{max.}$ 1232 cm.$^{-1}$ (aromatic ether).

Poly-[p,p′-*sulphonyldi*(*phenylmethylene*)] (IIb).—Phenyl-lithium (5·0 g.) in ether (250 ml.) was added dropwise to a refluxing solution of di-*p*-(bromomethyl)phenyl sulphone (12 g.) in ether (500 ml.) during 1 hr. The dark red-brown suspension was stirred for a further 15 min., decomposed by water (100 ml.), and just acidified. Filtration yielded a white solid which was washed with solvents and water (yield 7·4 g.), refluxed with 1 : 1 ethanol–concentrated hydrochloric acid (250 ml.) for 8 hr., washed with water and solvents, and dried, to give the *poly-sulphone* [Found: C, 68·2; H, 4·9; S, 13·2; Br, 0. $(C_{14}H_{12}O_2S)_n$ requires C, 68·8; H, 4·95; S, 13·1%] as a white powder (6·6 g., 90%), m. p. >360° (decomp.). This was almost completely insoluble, even in high-boiling aromatic solvents and had $\nu_{max.}$ 1151s, 1300s, 1318s (SO_2), 2857, 2926 (CH stretch). Di-*p*-tolyl sulphone had $\nu_{max.}$ 1148s, 1153s, 1294s, 1304s, 1319s, 2862, 2871, 2923, 2954.

Reaction of 4,4′-*Di*(*bromomethyl*)*benzophenone with Phenyl-lithium*.—Phenyl-lithium (2·77 g.) in ether (250 ml.) was added dropwise during 1 hr. to the bromo-compound (6 g.) in 1 : 1 benzene–ether (600 ml.) at 40°. The mixture was then decomposed by 10% acetic acid (150 ml.) and filtered (<0·1 g. of infusible solid). The organic layer was washed, dried, and concentrated to give a pale yellow oil (6·5 g.); the aqueous layer yielded no organic products. Repeated treatment of the oil with light petroleum (b. p. 60—80°) yielded a white solid (4·5 g.), m. p. 108—113°; recrystallisation (cyclohexane) of this 4,4′-*di*(*bromomethyl*)*triphenylmethanol* gave colourless rhombs (Found: C, 56·6; H, 3·9; Br, 32·7. $C_{21}H_{18}Br_2O$ requires C, 56·5; H, 4·0; Br, 35·8%), m. p. 121°; infrared analysis indicates the presence of OH (1153 and 3460 cm.$^{-1}$) and *p*-disubstituted benzene (1650—2000 cm.$^{-1}$), and absence of C=O. No reaction was effected between the starting material and lithium shavings in ether.

Di-p-*carboxyphenyl Ether*.—The method of Barrett *et al.*[22] led, in our hands, to impure mixtures of mono- and di-acid; instead, di-*p*-tolyl ether (17·1 g.), potassium permanganate (60 g.), and water (2 l.) were stirred and refluxed for 6 hr. The hot solution was filtered, cooled, and extracted with chloroform to remove unchanged ether (6·1 g.). The aqueous layer was concentrated to 1·5 l. and strongly acidified. The precipitate was filtered off and washed with water to give di-*p*-carboxyphenyl ether (8·5 g., 59%), m. p. 335—336° (equiv., 122·2. Calc., 129); the dimethyl ester formed needles (from benzene), m. p. 157° (Tomita[26] gives m. p. 153°).

The di-acid (5·148 g.) was dissolved in acetic anhydride (10 ml.) and heated at 280°/11 mm. for 2 hr. The residue (4·877 g.) was heated for 1 day at 280° and for 3 days at 280°/10^{-3} mm. The *poly-anhydride* [Found: C, 69·3; H, 3·6. $(C_{14}H_8O_4)_n$ requires C, 70·0; H, 3·4%], obtained as a tan powder (4·741 g.), softening pt. 320—322°, was soluble in benzyl benzoate but not in low-boiling solvents and was decomposed by sulphuric acid.

Reaction of 4-*Bromobenzyl Bromide with Butyl-lithium*.—Butyl-lithium (7·74 g.) in ether (250 ml.) was added dropwise during 20 min. to a stirred solution of 4-bromobenzyl bromide[27] (33 g.) in ether (200 ml.) at −30°. The solution was allowed to warm to room temperature and then refluxed for 8 hr. Treatment with methanol (20 ml.) and 5% hydrochloric acid (600 ml.) gave a clear solution. Extraction with ether gave a yellow oil (28 g.). Distillation of the oil yielded 1-bromo-4-pentylbenzene (7·1 g., 24%), b. p. 147—148°/19 mm., $n_D^{20·5}$ 1·5302, and 4,4′-dibromobibenzyl (11·1 g., 49%), b. p. 200—300°/19 mm., needles (from ethanol), m. p. 114—116°, undepressed on admixture with a specimen prepared by bromination of bibenzyl.[28]

The author thanks Mr. J. R. C. Duke for the *X*-ray powder photographs and Dr. R. L. Williams for determination of the infrared spectra.

Explosives Research and Development Establishment,
Ministry of Aviation, Waltham Abbey, Essex. [*Received, August 22nd,* 1960.]

[26] Tomita, *J. Pharm. Soc. Japan*, 1937, **57**, 609.
[27] Shoesmith and Slater, *J.*, 1926, 214.
[28] Stelling and Fittig, *Annalen*, 1866, **137**, 267.

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314. *Some Acetamide Complexes of the Actinide Tetrachlorides. Part I. Uranium, Neptunium, and Plutonium.*

By K. W. Bagnall, A. M. Deane, T. L. Markin, P. S. Robinson, and M. A. A. Stewart.

Ionic compounds of composition $MCl_4,6Ac{\cdot}NH_2$ (M = U, Np, or Pu) have been prepared in which the acetamide molecule is co-ordinated to the M^{4+} ion through the carbonyl-oxygen atom. Similar, but more stable, complexes with *NN*-dimethylacetamide, $MCl_4,2{\cdot}5Ac{\cdot}NMe_2$, have also been made; these are presumably dimeric.

The actinides from thorium to neptunium form well-defined tetrahalides, but the only known quadrivalent plutonium halide is the tetrafluoride. Thermodynamic evidence [1] indicates that the other simple quadrivalent plutonium halides cannot be prepared, but a few derivatives of the complex chloro-acid, H_2PuCl_6, have been recorded, notably the cæsium and the pyridinium salt which are readily precipitated from aqueous solution.[2]

It seemed probable that this cæsium salt could be used in the preparation of complexes of plutonium tetrachloride and that other dicæsium actinide hexachlorides might be useful starting materials, thus avoiding the handling problems associated with anhydrous actinide tetrachlorides, so much more hygroscopic than the dicæsium salts.

Experiments showed that the uranium analogue, Cs_2UCl_6, and diethylamine gave cæsium chloride (identified by *X*-ray powder photography) and what appeared to be a uranium tetrachloride–diethylamine complex, but the two could not be separated without the latter's decomposing. Since formamide and *NN*-dimethylformamide form complexes with titanium tetrachloride,[3] solid dicæsium hexachlorouranate(IV) was mixed with a boiling solution of acetamide in acetone; this gave a green solution of a uranium tetrachloride–acetamide complex, easily separated from the insoluble cæsium chloride. On cooling, the solution deposited a green oil or, more completely, on the addition of benzene or heptane. By repeated dissolution of the crude oil in hot acetone and precipitation with hydrocarbon, uncombined acetamide was removed, the product, after drying *in vacuo* at room temperature, being an emerald-green viscous oil, or oily solid, with a composition close to $UCl_4,6Ac{\cdot}NH_2$ ($Ac{\cdot}NH_2$: U = 5·70—5·90). On long storage over phosphorus pentoxide, it set to a green glass, m. p. ~60°, *d* 1·4.

The corresponding reddish-brown complexes $MCl_4,6Ac{\cdot}NH_2$ with neptunium and plutonium tetrachloride were made similarly. But whereas with the uranium and neptunium complexes acetone (4—5% by weight) was strongly held after prolonged drying *in vacuo*, the plutonium compound lost nearly all the excess of acetone under these conditions. As the complexes were found later to be thermally unstable, it seemed that preparation and purification in boiling acetone (56·5°) might be responsible for their slightly low acetamide content. Accordingly, ethanol was used; in this the complexes dissolve readily at room temperature and can be precipitated with isopentane or, less completely, benzene. It was found that ethanol was strongly held, but the ligand : uranium ratio was much improved. Retention of the solvent is presumably due to hydrogen-bonding with the amide-hydrogen.

The infrared spectra of the uranium complexes prepared by the acetone and by the ethanol route were identical, apart from absorptions due to the solvent.

Thermal degradation of the complexes in a vacuum on a quartz-fibre spiral thermobalance gave the curves in Fig. 1. The uranium complex appears to give a succession of

[1] Brewer, Bromley, Gilles, and Lofgren, "The Transuranium Elements," Nat. Nuclear Energy Series, ed. Seaborg, Katz, and Manning, McGraw-Hill Book Co., Inc., New York, 1949, Vol. IV—14B, p. 873.

[2] Anderson, ref. 1, p. 793.

[3] Dormer and Fernelius, *Z. anorg. Chem.*, 1934, **221**, 83; Archambault and Rivest, *Canad. J. Chem.*, 1958, **36**, 1461.

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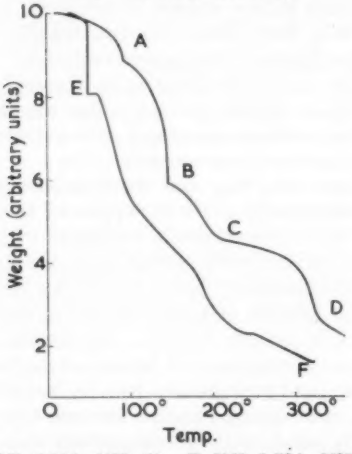
lower complexes with, presumably, four, three, and two mols. of adduct and, finally, uranium tetrachloride, but the lower complexes could not be isolated. Neptunium and plutonium complexes lose acetamide continuously without definite evidence of an intermediate complex or, for the plutonium complex, of the point at which chlorine is lost to give the trichloride. Consequently, although a uranium complex can be prepared by treating dicæsium hexachlorouranate(IV) with molten acetamide, in which the complex dissolves, the high temperature required for removal of the excess of acetamide in a vacuum leads to products of very variable composition.

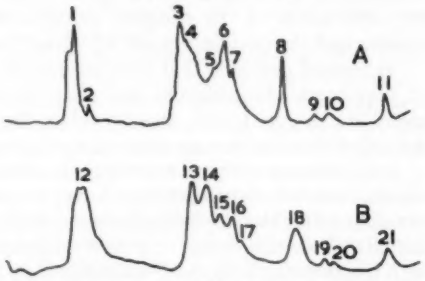
The uranium, neptunium, and plutonium complexes are soluble in hot acetone, methanol, ethanol, acetic acid, and acetic anhydride, but not in other organic solvents.

FIG. 1.
Thermal degradation of (A—D) UCl_4,6Ac·NH_2 *and* (E—F) $PuCl_4$,6Ac·NH_2.



A, UCl_4,5·35Ac·NH_2 (?). B, UCl_4,3·72Ac·NH_2 (?). C, UCl_4,3Ac·NH_2 (?). D, UCl_4,1·86Ac·NH_2 (?). E, $PuCl_4$,4·5Ac·NH_2 (?). F, $PuCl_3$.

FIG. 2. *Infrared spectra of* (A) *acetamide and* (B) UCl_4,6Ac·NH_2.



Maxima (cm.$^{-1}$): 1, 3305, 3160 (NH); 2, 2815 (Me); 3, 1680 (C=O); 4, 1636 (δ H–N–H); 5, 1459 (δa Me); 6, 1400 (δ NH_2); 7, 1356 (δs Me); 8, 1152 (NH_2?); 9, 1048; 10, 1006; 11, 874 (C–C–N); 12, 3310, 3165 (NH); 13, 1652 (δ N–N–H); 14, 1560 (C=O); 15, 1477 (δa Me); 16, 1410 (δ NH_2); 17, 1364 (δs Me); 18, 1140 (NH_2?); 19, 1050; 20, 1023; 21, 890 (C–C–N?).

They are all hygroscopic and decomposed by water. Although the complexes are precipitated from acetic acid or acetic anhydride by hydrocarbons, the composition of the product is variable. Possibly some acetylation of the amide group occurs under these conditions, for uranium tetrachloride certainly forms a complex with diacetimide.

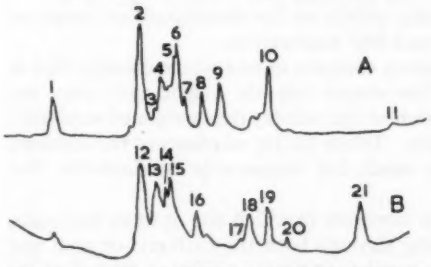
The infrared spectrum of the uranium tetrachloride complex is very similar to that of acetamide [4] (Fig. 2). In an attempt to assign the nearly coincident carbonyl stretching frequency and the H–N–H deformation band, the analogous complex with *NN*-dideuteroacetamide was prepared, but as the only solvents, acetone and ethanol, readily exchange hydrogen for deuterium, only about 50% of the original deuterium remained in the final product. The carbonyl-frequency shift ($\Delta\nu$ 120 cm.$^{-1}$) observed indicates strong bonding, being similar to that given by Susz [5] for ketonic carbonyl–metal bonding. There is also an extra band at 640 cm.$^{-1}$, possibly due to a U ◄— O stretching frequency or to the carbonyl-deformation frequency, since neither has been identified elsewhere. Thus the acetamide molecules appear to be co-ordinated to U^{4+} through the carbonyl-oxygen atom. This accords with the chemical evidence, for we have been unable to prepare complexes of uranium tetrachloride with either thioacetamide (where the sulphur-to-uranium co-ordination would be expected to be by a much weaker bond) or with α-chloroacetamide (where

[4] Spinner, *Spectrochim. Acta*, 1959, **15**, 95.
[5] Susz, *Helv. Chim. Acta*, 1958, **41**, 634.

the electron density at the carbonyl-oxygen atom would be much reduced by the electrophilic halogen atom). Further, phthalimide did not form a complex with uranium tetrachloride, possibly for steric reasons.

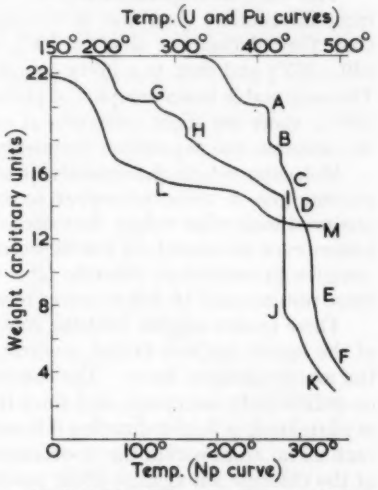
The uranium tetrachloride–acetamide complex is readily hydrolysed to products of indefinite composition which are insoluble in organic solvents. Thus it desiccates the organic solvents used in its preparation. It is fairly resistant to oxidation to uranium(VI), being unaffected by air at 190° or, in solution in acetone, by dry chlorine at 50°, but it is slowly oxidised to sexivalent uranium by ether peroxides. This behaviour differs little from that of uranium tetrachloride. Uranyl chloride–acetamide complexes are also formed, but have not yet been investigated.

FIG. 3. *Infrared spectra of* (A) NN-*dimethylacetamide and* (B) UCl_4,2·5Ac·NMe_2.



Maxima (cm.$^{-1}$): 1, 2925; 2, 1647; 3, 1548; 4, 1499; 5, 1410; 6, 1397; 7, 1355; 8, 1266; 9, 1189; 10, 1013; 11, 734; 12, 1618; 13, 1493; 14, 1427; 15, 1403; 16, 1252; 17, 1062; 18, 1032; 19, 974; 20, 917; 21, 753.

FIG. 4. *Thermal degradation of complexes* MCl_4,2·5Ac·NMe_2: A—F, M = Np; G—K, M = U; L—M; M = Pu.



A, $NpCl_4$,1·5Ac·NMe_2; B, $NpCl_4$,Ac·NMe_2; C, ($NpCl_4$,0·5Ac·NMe_2); D, $NpCl_4$; E—F, evapn. of $NpCl_4$. G, UCl_4,1·5Ac·NMe_2; H, UCl_4,Ac·NMe_2 (?); I, UCl_4; I—K, evapn. of UCl_4. L, $PuCl_4$,0·5Ac·NMe_2; M, $PuCl_3$.

The electrical conductivity of the uranium tetrachloride–acetamide complex in acetone shows it to be more ionised than uranium tetrachloride in the same solvent ($\chi_{complex}/\chi_{UCl_4}$ = 1·48, 0·0313M-solutions). Migration experiments with solutions in acetone–anhydrous acetic acid proved that U^{4+} ion and acetamide accumulated at the cathode, and chloride ion at the anode. The complex is presumably ionic, the cation consisting of a U^{4+} ion surrounded by 6 molecules of acetamide co-ordinated through the carbonyl-oxygen atom, thus explaining the insolubility in most organic solvents. All the chloride ions are replaced by nitrate or perchlorate ions by metathesis with a silver salt in acetone or ethanol. These new compounds of tetrapositive uranium and its simple nitrate and perchlorate, which we have made from acetone solutions of uranium tetrachloride, will be further investigated. It may also be possible to prepare the plutonium tetrabromide and tetraiodide complexes by similar procedures.

NN-Dimethylacetamide complexes have also been prepared by treating the dicæsium actinide hexachlorides with the substituted amide in acetone; the electron density at the nitrogen atom should here be much enhanced by the two methyl groups and it is not surprising that a new series of complexes emerged. These had the composition

$MCl_4,2{\cdot}5Ac{\cdot}NMe_2$ ($M = U^{4+}$, green; Np^{4+} and Pu^{4+}, red-brown in large crystals, yellowish-brown when finely divided), in which the M^{4+} cation may be co-ordinated to both the carbonyl-oxygen and the amide-nitrogen atom. These complexes are more stable than the simple acetamide derivatives and can readily be recrystallised from acetone. They are not hygroscopic, retain little, if any, organic solvent after drying *in vacuo* and, when recrystallised from acetone, melt sharply [U(IV), 182°; Np(IV), 181°; Pu(IV), 171°; all determined in sealed tubes; molten Np(IV) and Pu(IV) complexes are dark red]. They are soluble in the same solvents as the simple acetamide complexes and also in methylene chloride.

The infrared spectrum of the uranium complex (Fig. 3) is a highly distorted *NN*-dimethylacetamide spectrum. The shift of only about 30 $cm.^{-1}$ in the carbonyl frequency suggests a rather weaker U ◄— O bonding than in the acetamide complex.

The thermal degradation of the *NN*-dimethylacetamide derivatives in a vacuum is more informative than that of the simple acetamide complexes; the curves (Fig. 4) show that they decompose first to $MCl_4,1{\cdot}5X$ ($X = Ac{\cdot}NMe_2$) ($M = U^{4+}$, 245—275°; Np^{4+} 240—265°) and then to a lower complex MCl_4,X ($M = U^{4+}$ 315—325°; Np^{4+}, 268—278°). The only stable lower complex of plutonium tetrachloride appears to be $PuCl_4,0{\cdot}5X$ (290—370°); there are slight inflexions at corresponding points on the decomposition curves of the uranium and neptunium complexes at 370° and 290° respectively.

Molecular-weight determinations of the uranium complex in methylene chloride and in acetone give a value somewhat in excess of the simple formula weight and, since the observed molecular weight decreases with dilution of the solute, the compound evidently ionises even in solvents of low dielectric constant. Dilute (M/18) solutions of the uranium complex in methylene chloride ($D \sim 9$) had a small, but measurable conductivity, but these results could be due to traces of water.

These results suggest that the complex has a structure in which one or more molecules of the ligand act as a bridge, co-ordination being through both the carbonyl-oxygen and the amide-nitrogen atom. The compounds are non-hygroscopic, indicating that they are co-ordinatively saturated, and since it is unlikely that quadrivalent uranium, neptunium, or plutonium is 5-co-ordinating it is possible that one or more chlorine atoms are bonded to each metal atom within the co-ordination sphere. In such a case, potentiometric titration of the chloride ion against silver perchlorate in acetone solution should reveal an inflexion at the point where the free chloride ion, external to the co-ordination sphere, has all been replaced by perchlorate ion, but no intermediate step in the titration curve could be observed experimentally. This may only mean that the chloride ion within the co-ordination sphere is extremely labile.

Experimental

Owing to its long half-life ($2{\cdot}2 \times 10^6$ years) ^{237}Np can be safely handled in 100 mg. amounts in a well-ventilated fume-hood. Experimental work with plutonium was done in a glove-box to minimise the hazards of a highly radioactive material. Natural uranium presents little radioactive danger.

Preparative.—(a) *Dicæsium actinide hexachlorides.* The salts were prepared by dissolving the appropriate tetrachloride (Th, U) in hydrochloric acid, adding cæsium chloride, and slowly evaporating the solution under reduced pressure at room temperature,[6] or by adding cæsium chloride in 6N-hydrochloric acid to a solution of the quadrivalent actinide (Np, Pu) in 6N-hydrochloric acid and filtering off the precipitate (cf. Anderson [2]). We found it convenient to mix solutions of the quadrivalent actinide (U, Np, Pu) and cæsium chloride in 2—11N-hydrochloric acid and to saturate the mixture with hydrogen chloride; precipitation of the complex salt is almost complete. The purity of the products was established by chemical analysis and their identity confirmed by *X*-ray powder photography.

The solutions of the quadrivalent actinides were prepared as follows:

(1) Uranium(IV). By cathodic reduction of uranyl chloride in dilute hydrochloric acid, by

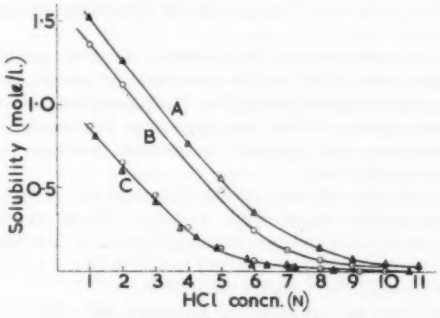
[6] Ferraro, *J. Inorg. Nuclear Chem.*, 1957, **4**, 283.

the reduction of uranyl chloride in 6N-hydrochloric acid with aluminium or with scrap metallic uranium, or by dissolving metallic uranium in concentrated hydrochloric acid; the uranium(III) first formed in the last three operations is rapidly oxidised to uranium(IV) on storage in the cold. Reduction with aluminium gives a dicæsium salt contaminated with a cæsium aluminium chloride.

(2) Neptunium(IV). By reducing a cold stock solution of Np(V)/Np(IV) (~0·5 g.) in 5N-nitric acid with hydrazine; the fawn quadrivalent hydroxide was precipitated with aqueous ammonia and, after being washed thrice with water, was dissolved in 6N-hydrochloric acid. The reduction cycle was repeated and the hydroxide redissolved in concentrated hydrochloric acid. Since the procedure occasionally gave erratic yields, later preparations were made by reduction with iodide ion (ammonium iodide) which always gave satisfactory results.

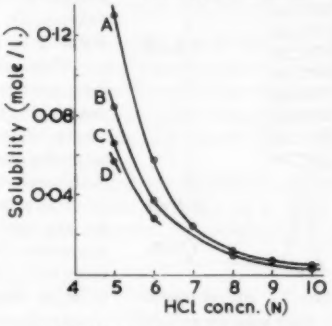
(3) Plutonium(IV). By boiling a solution of plutonium (1 g.) with concentrated nitric acid to break up the colloidal Pu(IV), and reduction to Pu(III) with formaldehyde, which also removed the excess of nitric acid; some concentrated hydrochloric acid was added to maintain acidity. Plutonium(III) hydroxide was precipitated with aqueous potassium hydroxide, and the precipitate, after being washed with water, was redissolved in concentrated hydrochloric acid

FIG. 5. *Solubility of* $CsMCl_6$ *in hydrochloric acid*: A, M = U, *at* 25°; B, M = Np, *at* 18°; C, M = Pu, *at* 25°.



△, *Data from ref.* 9. ○, *This work.*

FIG. 6. *Effect of added cæsium chloride on the solubility of dicæsium hexachloroplutonate in hydrochloric acid.*



Added CsCl: A, nil; B, 0·05M; C, 0·10M; D, 0·15M.

and oxidised to plutonium(IV) with aqueous hydrogen peroxide. Completion of the oxidation was indicated by a colour change from bluish-violet to reddish-brown.

(b) *Amide complexes.* The appropriate dicæsium salt was stirred with a five-fold excess of acetamide in hot acetone or cold ethanol, the insoluble cæsium chloride was filtered off, and the complex precipitated from the filtrate by the addition of benzene, heptane, or isopentane. As the hydrocarbon was immiscible with high acetamide concentrations (>200 mg./ml.) the solution was diluted with solvent until miscibility was achieved. The reaction in ethanol was exothermal. The precipitated complex was redissolved in hot acetone or cold ethanol, and precipitation and redissolution were repeated four times to remove the excess of acetamide. The excess of hydrocarbon was evaporated in a current of dry air at room temperature and the oily product dried at 10^{-5} mm. for several hours. Ethanol is preferred as a solvent for the acetamide complexes, but acetone is better for the *NN*-dimethylacetamide complexes and was always used for them. Isopentane is the most convenient precipitant since its low b. p. makes removal easy.

Preparation of the *NN*-dimethylacetamide complexes was similar to that of the acetamide complexes in the first stages, but after the final precipitation the complex was crystallised from acetone. These crystals were collected, dried at 10^{-5} mm., powdered, and again dried in a vacuum.

(c) NN-*Dideuteroacetamide.* Pure trideuteroammonia was prepared by Hart and Partington's method [7] and liquefied in a trap, cooled in solid carbon dioxide–ethanol, containing

[7] Hart and Partington, *J.*, 1943, 104.

redistilled ethyl acetate. Redistilled acetyl chloride, from which any hydrogen chloride had been displaced by a stream of dry nitrogen at 0°, was added dropwise to the liquid ND_3–ethyl acetate mixture until reaction was complete. The product was extracted in 1 : 1 benzene–ethyl acetate in a closed system in which the solvent could be recirculated by suction.

(d) *Acetamide.* B.D.H. reagent-grade material was recrystallised from ethanol and dried *in vacuo*.

(e) NN-*Dimethylacetamide.* B.D.H. reagent-grade material was fractionated under reduced pressure, the middle, constant-boiling fraction being used.

(f) *Solvents.* Alcohols were dried by refluxing over freshly prepared barium oxide and distilled. Benzene was dried over sodium. Acetone was dried to some extent over magnesium nitride. Rigorous drying of the solvents appears to be unnecessary, however, since some of the preparation can be sacrificed as insoluble hydrolysis products.

Solubilities.—The solubility curves of the dicæsium hexachloro-uranate(IV) and -plutonate in hydrochloric acid, and the method for their determination, have been recorded;[8] the plutonium work has been repeated, with good agreement, and the curve for the neptunium analogue has also been obtained (Fig. 5). The effect of an excess of cæsium chloride on the solubility of dicæsium hexachloroplutonate is shown in Fig. 6.

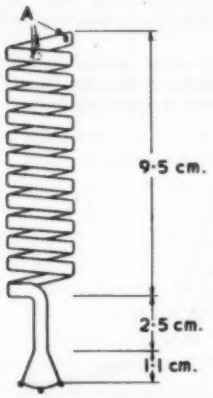


FIG. 7. *Spiral pump.*
(A, *Exit holes for pumped liquid.*)

Thermogravimetric Data.—These were obtained with a conventional quartz fibre thermo-balance (sensitivity 4·5 mg./cm. extension); the heating rate was 2°/min. and the operating pressure 0·02—2×10^{-6} mm.

Molecular-weight Determinations.—The standard Cottrell method had too much temperature drift to give reproducible results in a reasonable time and a simple spiral pump (Fig. 7) replaced the Cottrell pump after it had been tested. With this apparatus the results for naphthalene, benzophenone, and biphenyl in benzene, acetone, and dichloromethane were ~1·5% low.

The apparatus requires 30—60 min. for equilibration, but is simple to use and gives reasonably reproducible results. Those for the uranium *NN*-dimethylacetamide complex in methylene chloride ranged from 673 (14·8 g. of complex per kg. of solvent) to 625 (6·49 g./kg.), the formula weight of the monomeric complex being 598.

Analysis.—(a) *Chloride ion.* A weighed quantity (50—100 mg.) of the neptunium orplutonium compound was treated with dilute aqueous potassium hydroxide and the precipitated actinide hydroxide separated by centrifugation. The supernatant liquid was acidified with nitric acid, an equal volume of acetone added, and the chloride ion determined potentiometrically against silver nitrate. Addition of acetone markedly increases the sharpness of the end-point. The metal component was not separated from the uranium complex since its recovery is not obligatory.

(b) *Uranium.* Uranium(IV) was determined volumetrically by titration to uranium(VI) with dichromate,[9] and samples were checked for the presence of uranium(VI) by reduction on a lead column in 3N-hydrochloric acid,[10] but it was never found.

(c) *Neptunium and plutonium.* ^{237}Np and ^{239}Pu were determined by α-counting aliquot parts of a solution of the complex. Samples were also subjected to α-pulse analysis in order to ascertain the isotopic composition of the material and detect α-emitting impurities. The neptunium proved to contain 0·02 weight % of ^{239}Pu, and allowance was made for the α-emission from this relatively short-lived isotope.

The weights of neptunium and plutonium were calculated with $1 \cdot 562 \times 10^6$ disintegrations $min.^{-1}$ $mg.^{-1}$ as the specific activity of ^{237}Np and $1 \cdot 38 \times 10^9$ dis. $min.^{-1}$ $mg.^{-1}$ as that of ^{239}Pu.

(d) *Acetamide.* The amide content of the complexes was determined from a nitrogen analysis by the Kjeldahl method, the *NN*-dimethylacetamide complexes being subjected to a preliminary digestion in concentrated sulphuric acid.

[8] Kooi, Weisskopf, and Gruen, *J. Inorg. Nuclear Chem.*, 1960, **13**, 310.
[9] Cf., *e.g.*, Rodden and Warf, "The Analytical Chemistry of the Manhattan Project," Nat. Nuclear Energy Series (ed. Rodden), McGraw-Hill Book Co., Inc., New York, N.Y., 1950, Vol. VIII—1, p. 68.
[10] Sill and Peterson, *Analyt. Chem.*, 1952, **24**, 1175.

(e) *Carbon.* Combustion analysis was attempted but the results were vitiated by the presence of organic solvent.

(f) *Results.* Owing to the retention of solvent, the results (tabulated) for the simple acetamide complexes are expressed as ligand : metal and chloride : metal ratios.

	$Ac{\cdot}NH_2/M(IV)$ Found	$Cl^-/M(IV)$ Found	Solvent impurity
$UCl_4.6Ac{\cdot}NH_2$	6·02	4·04	4—22% (*a*)
$NpCl_4.6Ac{\cdot}NH_2$	6·22	4·04	~2% (*a*)
$PuCl_4.6Ac{\cdot}NH_2$	5·88	3·97	~2% (*b*)

(*a*) Ethanol. (*b*) Acetone.

	M(IV) (%)		Cl^- (%)		$Ac{\cdot}NMe_2$ (%)	
	Found	Reqd.	Found	Reqd.	Found	Reqd.
$UCl_4.2{\cdot}5Ac{\cdot}NMe_2$	39·5	39·8	23·8	23·7	35·8	36·5
$NpCl_4.2{\cdot}5Ac{\cdot}NMe_2$	39·6	39·7	23·9	23·8	35·7	36·5
$PuCl_4.2{\cdot}5Ac{\cdot}NMe_2$	40·5	39·9	21·5	23·7	36·7	36·4

Analyses of the plutonium compound were not very satisfactory, but spectrophotometric examination of solutions of the freshly prepared complex in dilute hydrochloric acid confirmed that the plutonium was nearly all (99%) in the quadrivalent state, the remaining 1% being plutonium(VI). In addition, *X*-ray powder photography showed that the plutonium compound was isostructural with its uranium and neptunium analogues; the reason for the low analytical results is unknown.

X-Ray Powder Photography.—Powder photographs were taken with a 19 cm. Unicam Debye–Scherrer camera and filtered Cu-K_α radiation. The *NN*-dimethylacetamide complexes all gave quite good *X*-ray diffraction patterns, but the complexes are evidently of low symmetry, probably monoclinic or triclinic. The uranium, neptunium, and plutonium compounds are isostructural, and the uranium compound may undergo a phase change above 180°. The crystallography of these compounds has not been further investigated.

Infrared Spectra.—Spectra of the acetamide complex were observed for very thin capillary films or melts, and the uranium tetrachloride–*NN*-dimethylacetamide complex as a melt in Fluorube and Nujol; a Hilger H800 spectrometer with sodium chloride, potassium bromide, and cæsium bromide prisms was used.

The authors thank Mrs. K. M. Glover for carrying out the α-pulse analysis.

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DIDCOT, BERKS. [*Received, August 29th,* 1960.]

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315. *Thiadiazoles. Part XI.* Synthesis and Cyclisation of N-(Thiobenzamido)guanidines and Related Compounds.*

By FREDERICK KURZER.

N-Thiobenzamido-guanidine, -urea, and -thiourea and their *N'*-phenyl-analogues are synthesised by thiobenzoylation of the appropriate hydrazino-compounds. They are readily cyclised in acid media to a variety of substituted 1,3,4-thiadiazoles in excellent yield.

AMINOGUANIDINE reacts with isocyanate and isothiocyanate esters, at either its hydrazino-[1] or its amidino-group,[2] to yield substituted ureas or thioureas which are versatile starting materials in heterocyclic syntheses (for summary see ref. 2). Condensation products of the general structure $R{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}C(:NH){\cdot}NH{\cdot}NH_2$, for example, have recently been converted, by hydrolytic or oxidative cyclisation, into substituted 1,2,4-triazoles[2] or 1,2,4-thiadiazoles,[3] respectively. In this connexion, the examination of analogous

* Part X, *J.*, 1960, 3240.

[1] Fantl and Silbermann, *Annalen*, 1928, **467**, 281; Fry and Lambie, B.P. 741,228, 741,280/1955.
[2] Godfrey and Kurzer, *J.*, 1960, 3437.
[3] Godfrey and Kurzer, *J.*, unpublished work.

reactions of simpler related structures that would result from the thioacylation of aminoguanidine appeared of interest.

Amongst thioacylating agents,[4] (thiobenzoylthio)acetic acid, first prepared by Holmberg[5,6] in 1944, has proved particularly useful in thiobenzoylating amino-acids[6-9] and hydrazine derivatives.[5,6-10] In studies concerning nickel-complexing agents related to thiosemicarbazide,[11] Jensen and Miquel[8] described products obtained by thiobenzoylating aminoguanidine, semicarbazide, and thiosemicarbazide with this reagent.

$Ph{\cdot}CS{\cdot}NH{\cdot}NH{\cdot}C(:NH){\cdot}NH_2$ (II) $NH_2{\cdot}N(Ph{\cdot}CS){\cdot}C(:NH){\cdot}NH_2$ (IIa) $NH_2{\cdot}NH{\cdot}C(:NH){\cdot}NH{\cdot}CS{\cdot}Ph$ (IIb)

Aminoguanidine (I) and sodium (thiobenzoylthio)acetate reacted in aqueous solution at room temperature, under the conditions of Holmberg's general procedure,[5,6] to afford good yields of *N*-(thiobenzamido)guanidine (II), together with small quantities of 2,5-diphenyl-1,3,4-thiadiazole (IX). The guanidine derivative (II) differed materially from Jensen and Miquel's product[8] (m. p. 146—147°, from water), in forming a hemihydrate (m. p. 164—166°) when crystallised from water, or the anhydrous base (m. p. 180—182°) from organic solvents. Three isomeric thiobenzoyl derivatives (II, IIa, IIb) of aminoguanidine are theoretically possible; the formulation of the product as (II) is based on the marked difference in the reactivity of hydrazino- and guanidino-groups towards (thiobenzoylthio)acetic acid. Thus, structure (IIb) may be rejected because aminoguanidine having its hydrazino-group blocked (*e.g.*, X) failed to yield a thiobenzoyl derivative. Guanidine itself is known to react only very incompletely with other thiobenzoylating agents[12] and hardly at all with (thiobenzoylthio)acetic acid.[9] Although methylhydrazine is attacked at the methylamino-group[10] (to yield $Ph{\cdot}CS{\cdot}MeN{\cdot}NH_2$), a comparable structure (IIa) for the present compound is excluded by the results of cyclisation experiments, which are readily interpreted in terms of structure (II) but are not compatible with (IIa).

In agreement with its constitution, *N*-(thiobenzamido)guanidine (II) displays both acidic and basic properties, dissolving in alkalis or acids, and forming a picrate. Alkylation gave products, which evolved alkanethiol on hydrolysis and are therefore formulated as *S*-alkylthio-derivatives (VIII; R′ = Et or $Ph{\cdot}CH_2$). Boiling hydrochloric acid or acetic anhydride rapidly cyclised the compound (II), with loss of ammonia. to 2-amino-5-phenyl-1,3,4-thiadiazole (XI) or the corresponding acetyl derivative (XII). These results are complementary to the analogous ring-closure of *N*-(thiobenzamido)urea (III) and thiourea (IV) to 2-hydroxy(or mercapto)-5-phenyl-1,3,4-thiadiazole described by Lawson and Searle.[9] Treatment of *N*-(thiobenzamido)guanidine (II) with alkalis, however, did not eliminate the elements of hydrogen sulphide to yield 1,2,4-triazoles, which are readily obtained from the structurally related *N*-(thioureido)guanidines,[1] but resulted merely in hydrolysis to *N*-(thiobenzamido)urea (III). In this respect, the compound (II) behaved as the parent aminoguanidine (I), which is converted chiefly into semicarbazide[13] on alkaline hydrolysis.

The wider applicability of the synthesis, and the consistent behaviour of compounds of types (V—VII) was apparent from an examination of the aryl derivatives. Thiobenzoylation of 1-amino-3-phenylguanidine, and its 3-*p*-tolyl homologue, gave the expected 1-aryl-3-(thiobenzamido)guanidines (V; R = Ph or p-C_6H_4Me) in moderate yields. A

[4] McOmie, *Ann. Reports*, 1948, **45**, 207.
[5] Holmberg, *Arkiv Kemi, Min., Geol.*, 1944, **17**, *A*, No. 23.
[6] Holmberg, "Svedberg Memorial Volume," Uppsala, 1944, p. 299.
[7] Elliott, *Nature*, 1948, **162**, 658; Kjaer, *Acta Chem. Scand.*, 1950, **4**, 1347; Crawhall and Elliott, *J.*, 1951, 2071; Kjaer, *Acta Chem. Scand.*, 1952, **6**, 1374; Jepson, Lawson, and Lawton, *J.*, 1955, 1791.
[8] Jensen and Miquel, *Acta Chem. Scand.*, 1952, **6**, 189.
[9] Lawson and Searle, *J.*, 1957, 1556.
[10] Holmberg, *Arkiv Kemi*, 1956, **9**, 47.
[11] Jensen, *Z. anorg. Chem.*, 1934, **219**, 243; 1934, **221**, 6, 11.
[12] Goerdeler and Fincke, *Chem. Ber.*, 1956, **89**, 1033.
[13] Thiele, *Annalen*, 1892, **270**, 1; Lieber and Smith, *J. Amer. Chem. Soc.*, 1937, **59**, 2283; *Chem. Rev.*, 1939, **25**, 213, 226.

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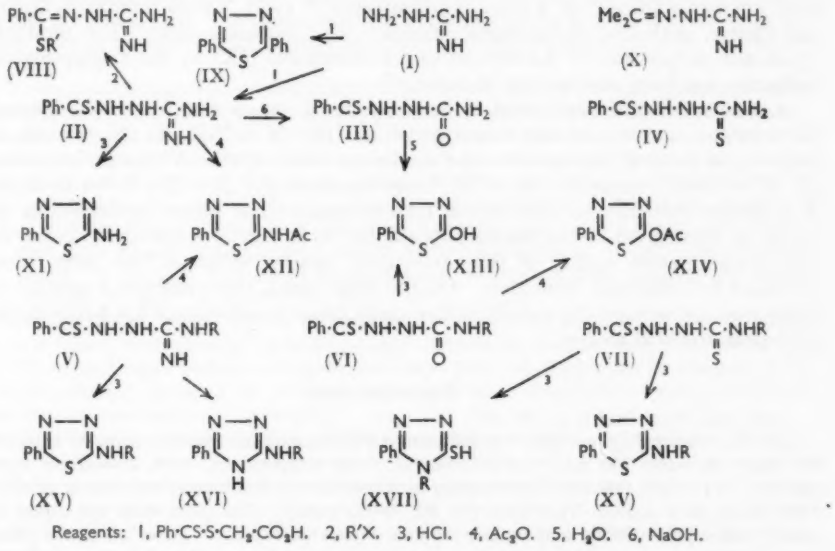
by-product of this reaction is formulated, on the basis of its origin, composition, and molecular weight, as 3-anilino-5-phenyl-1,2,4-triazole (XVI), being formed (from V) by loss of hydrogen sulphide and cyclisation. This representation of the product, rather than the alternative 3-amino-4,5-diphenyl-1,2,4-triazole structure, is preferred on the assumption that an amino- rather than anilino-group is involved in the cyclisation. Like its prototype (II), 1-phenyl-3-(thiobenzamido)guanidine (V; R = Ph) was not cyclised to the 1,2,4-triazole by strong alkalis, from which it was recovered even after prolonged boiling. In acid media, on the other hand, cyclisation occurred rapidly and completely; in mineral acid it gave the expected 2-anilino-5-phenyl-1,3,4-thiadiazole (XV; R = Ph), whilst with acetic anhydride, eliminating aniline instead of ammonia, it yielded 2-acetamido-5-phenyl-1,3,4-thiadiazole (XII).

4-Phenyl-1-(thiobenzoyl)semicarbazide (VI), the oxygen analogue of the series, was readily produced in good yield, together with small quantities of 2,5-diphenyl-1,3,4-



thiadiazole (IX) as by product, by the general reaction. The compound was unaffected by alkalis, in which it was soluble. In contrast with the reaction of (V), elimination of a basic component by acidic reagents from (VI) can occur in one way only; accordingly, both hydrochloric acid and acetic anhydride cyclised the semicarbazide (VI), with loss of aniline, to 2-hydroxy(or acetoxy)-5-phenyl-1,3,4-thiadiazole (XIII, XIV).

Thiobenzoylation of 4-phenyl(thiosemicarbazide) occurred in the normal way in good yield; the expected product (VII; R = Ph) could not be characterised, however, because it cyclised spontaneously (to XVII) when attempts were made to isolate it. Under the influence of mineral acid, ring-closure occurred nearly quantitatively, with elimination of hydrogen sulphide, and proceeded along two routes simultaneously to yield mixtures of 3-mercapto-4,5-diphenyl-1,2,4-triazole (XVII; R = Ph) and 2-anilino-5-phenyl-1,3,4-thiadiazole (XV; R = Ph), the former predominating. It is noteworthy that in this case the usual elimination of the basic component by action of the acidic cyclising agent, resulting in the formation of 2-mercapto-5-phenyl-1,3,4-thiadiazole (as from IV [9]) does not occur. The reaction thus resembles closely the ready cyclodehydration of 1-benzoyl-4-phenyl(thiosemicarbazide), which affords varying proportions of the same products (XV

and XVII), either on pyrolysis,[14] or on treatment with phosphoric acid,[15] acyl chlorides,[14-16] or alkalis.[17]

In common with their parent compounds [8] (II—IV), the aryl-substituted analogues (V—VII) gave deep-brown nickel complexes; the *S*-alkyl derivatives (VIII), however, failed to do so. This observation is accounted for adequately by Jensen and Miquel's general formulation [8] of thiobenzhydrazide-nickel complexes of this type.

(A) Ph·CS·NH·NH·CX·NHR Ph·NH·CS·NH·NH·CX·NHR (B)

2,5-Diphenyl-1,3,4-thiadiazole (IX), formed as a by-product in the thiobenzoylation of aminoguanidine (I) and 4-phenylsemicarbazide, arises directly by a side-reaction. Thus, in the former case, it cannot originate from intermediate *N*-(thiobenzamido)guanidine (II), either in the alkaline environment, or during its recrystallisation, since reaction (of II) with alkali proceeds differently (yielding III), while even prolonged action of boiling water is without effect. It is probable that small quantities of hydrazine, formed hydrolytically from aminoguanidine [13] or 4-phenylsemicarbazide [18] yield *NN'*-di(thiobenzoyl)hydrazine, and thence, with loss of hydrogen sulphide, the thiadiazole (IX). The production of significant proportions of 2,5-diphenyl-1,3,4-thiadiazole (IX) in the thiobenzoylation of hydrazine has been observed by Holmberg.[5]

A comparison of the behaviour of the two series of compounds (A) and (B) demonstrates the increased stability of the former structures (A; X = :NH, :O, :S) towards alkalis; they are, in general, unaffected under conditions which cyclise *N*-(thioureido)-guanidines (B; X = :NH),[1] -ureas (B; X = :O),[19] and thioureas (B; X = :S), [19,20] with elimination of hydrogen sulphide, to substituted 1,2,4-triazoles. The higher resistance in alkaline media to elimination of the thiobenzoyl-sulphur over that of a thioureido-group may be due to the greater acidity of the thiobenzoyl moiety, which is thus more effectively stabilised by alkali-salt formation. On the other hand, there emerges a general parallel behaviour of structures (A) and (B) in their ring-closure to substituted 1,3,4-thiadiazoles [20,21] in neutral and acid media.

Experimental

Light petroleum had b. p. 60—80°.

N-(*Thiobenzamido*)*guanidine*.—A solution of aminoguanidine sulphate monohydrate (13·2 g., 0·1 mole) in water (50 ml.) was treated, at room temperature, with 3N-sodium hydroxide (33·3 ml., 0·1 mole), followed immediately by a solution of (thiobenzoylthio)acetic acid (15·9 g., 0·075 mole) in N-sodium hydroxide (75 ml., 0·075 mole). The clear deep red liquid became orange, later pale yellow, and yellow crystals separated rapidly. After 24 hours' storage at room temperature, and 6 hours' at 0°, the product was collected (12 g.) and crystallised from boiling water (15 ml. per g., insoluble residue: R), yielding needles of N-(*thiobenzamido*)*guanidine hemihydrate*, m. p. 164—166° (decomp.) (10·9 g., 72%) (Found: C, 48·0, 47·8; H, 5·1, 5·2; N, 28·0; S, 15·2. $C_8H_{10}N_4S,\frac{1}{2}H_2O$ requires C, 47·3; H, 5·4; N, 27·6; S, 15·8%). The use of an excess of (thiobenzoylthio)acetic acid (1·1 or 1·25 mol.) gave 56 and 64% yields (based on aminoguanidine) respectively, while an excess of aminoguanidine (2 mol.) raised yields to 80% [based on (thiobenzoylthio)acetic acid].

A specimen of the material (2 g.), suspended in boiling ether (10 ml.), was dissolved by the addition of hot methanol (6 ml.). The solution, diluted with more ether (20 ml.), slowly deposited prisms, which on drying gave a white powder of the anhydrous substituted *guanidine*,

[14] Marckwald and Bott, *Ber.*, 1896, **29**, 2914; Dymek, *Ann. Univ. Mariae Curie-Sklodowska*, 1954, **9**, *AA*, 61.
[15] Hoggarth, *J.*, 1949, 1166.
[16] Pulvermacher, *Ber.*, 1894, **27**, 622.
[17] Fromm and Trnka, *Annalen*, 1925, **442**, 156; Sugii, *Yakugaku Zasshi*, 1958, **78**, 283.
[18] Curtius and Heidenreich, *Ber.*, 1894, **27**, 56; *J. prakt. Chem.*, 1895, **52**, 465.
[19] Arndt, Milde, and Tschenscher, *Ber.*, 1922, **55**, 341.
[20] Arndt and Milde, *Ber.*, 1921, **54**, 2089, 2101.
[21] Freund, *Ber.*, 1894, **27**, 1774; 1895, **28**, 946; Busch and Schmidt, *Ber.*, 1913, **46**, 2240; Busch and Lotz, *J. prakt. Chem.*, 1914, **90**, 257.

m. p. 180—182° (decomp.) (Found: C, 49·2; H, 5·0; N, 29·4; S, 16·8. $C_8H_{10}N_4S$ requires C, 49·5; H, 5·15; N, 28·9; S, 16·5%). Jensen and Miquel [8] give m. p. 146—147°.

The compound was highly soluble in cold methanol, ethanol, and acetone, but sparingly soluble in boiling benzene, light petroleum, and ether. It dissolved in 2N-hydrochloric or acetic acid and in 2N-sodium hydroxide or ammonia. With alkaline sodium plumbite, it gave a white precipitate which remained unchanged on boiling.

The water-insoluble residue R (0·45—0·6 g.) consisted, after crystallisation from ethanol, of platelets of 2,5-diphenyl-1,3,4-thiadiazole, m. p. 138—140° (0·35 g., 4%) (Found: C, 70·6; H, 4·0; N, 11·7; S, 13·6. Calc. for $C_{14}H_{10}N_2S$: C, 70·6; H, 4·2; N, 11·8; S, 13·4%). Stolle [22] gives m. p. 141—142°.

N-(Thiobenzamido)guanidine hemihydrate was recovered almost quantitatively (on cooling) from its 5% aqueous solution which had been refluxed during 3 hr.

A solution of the hemihydrate (0·001 mole) in water (40 ml.) at 30° was treated with 0·05M-aqueous picric acid (0·001 mole). The yellow precipitate was dissolved in ethanol (10 ml.); the filtered solution deposited needles (0·05 g.) of 2-amino-5-phenyl-1,3,4-thiadiazole picrate, m. p. and mixed m. p. (see below) 256—258° (decomp.). The filtrate, on spontaneous evaporation to one-third bulk gave N-(*thiobenzamido*)*guanidine picrate*, m. p. 212—214° (decomp.), as an opaque orange powder (50%) (Found: C, 39·8; H, 2·9. $C_8H_{10}N_4S,C_6H_3N_3O_7$ requires C, 39·7; H, 3·1%).

N-(*Thiobenzamido*)*guanidine*.—S-*Ethyl derivative*. A solution of *N*-(thiobenzamido)guanidine hemihydrate (5·1 g., 0·025 mole) in ethanol (25 ml.)–ethyl bromide (13·6 g., 0·125 mole) was refluxed during 3 hr., another portion of ethyl bromide (0·125 mole) being added after 1·5 hr. The yellow liquid was concentrated *in vacuo* to small volume, and the remaining viscous liquid (approx. 15 ml.) diluted with water. The resulting clear liquid, on treatment with 3N-ammonia (10 ml.), gave an immediate precipitate of oil which solidified when stirred and kept. It was collected at 0°, dried, and crystallised from benzene containing 5% of methanol (50 ml.), and gave prisms (4·45 g., 80%) of the S-*ethyl derivative*, m. p. 142—144° [Found: C, 54·1; H, 6·3; N, 25·4; S, 14·8%; *M* (cryoscopically, in thymol), 220. $C_{10}H_{14}N_4S$ requires C, 54·05; H, 6·3; N, 25·2; S, 14·4%; *M*, 222].

The compound was highly soluble in methanol, ethanol, and acetone, soluble in boiling benzene and water, and sparingly soluble in light petroleum, cold benzene, and water. It evolved ethanethiol when boiled with 3N-hydrochloric acid. A 0·1M-aqueous solution of the *S*-derivative, refluxed during 2 hr., evolved only traces of ethanethiol, the compound being recovered almost quantitatively on cooling.

S-*Benzyl derivative*. A solution of *N*-(thiobenzamido)guanidine hemihydrate (2·03 g., 0·01 mole) in ethanol (10 ml.) was successively treated with benzyl chloride (1·9 g., 0·015 mole) and 3N-sodium hydroxide (3·3 ml., 0·01 mole). The clear liquid was kept at 60° during 30 min., concentrated to one-third bulk, and stirred into water (75 ml.). After 48 hours' storage, the precipitated oil had solidified and was collected. Crystallisation from chloroform–light petroleum (5 and 6 ml. per g.) gave platelets (2·0 g., 70%) of the S-*benzyl derivative*, m. p. 112—114° (Found: C, 63·7; H, 5·4; N, 19·7; S, 11·1. $C_{15}H_{16}N_4S$ requires C, 63·4; H, 5·6; N, 19·7; S, 11·3%). Alternatively, crystallisation from ethanol–light petroleum (b. p. 40—60°) (3 ml. each per g.) gave the white granular (2·65 g., 80%) *solvated derivative*, m. p. 132—134° (Found: C, 61·9; H, 5·9. $C_{15}H_{16}N_4S,C_2H_5{\cdot}OH$ requires C, 61·8; H, 6·7%). It evolved toluene-ω-thiol when boiled with 3N-hydrochloric acid or 3N-sodium hydroxide, followed by acidification.

N-(*Thiobenzamido*)*guanidine*.—(a) *Action of hydrochloric acid*. The reactant (hemihydrate; 1·02 g., 0·005 mole) was refluxed in 3N-hydrochloric acid (20 ml., 0·06 mole) during 15 min., the originally bright yellow solution becoming colourless within 1—2 min. The liquid was basified at room temperature, and the crystalline precipitate was collected at 0°, rinsed with a little water, and crystallised from acetone-ethanol (1 : 2), rectangular prisms of 2-amino-5-phenyl-1,3,4-thiadiazole, m. p. 222—224°, being obtained (total, 0·83 g., 93%) (Found: C, 54·7; H, 4·2; N, 24·2; S, 18·2. Calc. for $C_8H_7N_3S$: C, 54·2; H, 3·95; N, 23·7; S, 18·1%). Young and Eyre [23] give m. p. 222—223°. The picrate formed needles, m. p. 256—258° (decomp.) (from a large volume of ethanol) (Found: C, 41·3; H, 2·7. Calc. for $C_8H_7N_3S,C_6H_3N_3O_7$: C, 41·4; H, 2·5%). Lawson and Searle [9] give m. p. 268—271° (decomp.).

[22] Stolle, *Ber.*, 1899, **32**, 797; *J. prakt. Chem.*, 1904, **69**, 366.
[23] Young and Eyre, *J.*, 1901, **79**, 54.

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(b) *Action of acetic anhydride.* A suspension of the reactant (0·005 mole) in acetic anhydride (10 ml.) was heated to boiling and gave a clear yellow liquid which became colourless and deposited a copious white crystalline precipitate almost immediately. Heating at 100° was continued during 1 hr., the suspension stirred into water, and the crystalline product collected at 0°. Crystallisation from boiling ethanol (200 ml.) gave silky needles (1·0 g., 91%) of 2-acetamido-5-phenyl-1,3,4-thiadiazole, m. p. 276—278° (Found: C, 54·8; H, 4·0. Calc. for $C_{10}H_9N_3OS$: C, 54·8; H, 4·1%). Young and Eyre [23] give m. p. 276°.

N-(*Thiobenzamido*)*urea.*—(*a*) This compound, prepared in 90% yield according to the method of Jensen and Miquel,[8] formed pale-yellow needles (from water) or plates, m. p. 160—162° (decomp.) (from ethanol–light petroleum) (Found: C, 49·6; H, 4·8. Calc. for $C_8H_9N_3OS$: C, 49·2; H, 4·6%). Jensen and Miquel [8] give m. p. 155°.

(*b*) *N*-(Thiobenzamido)guanidine hemihydrate (3·05 g., 0·015 mole) in 3N-sodium hydroxide (30 ml., 0·09 mole) was refluxed during 30 min., ammonia being slowly evolved. The filtered nearly colourless liquid was acidified (to Congo Red) with concentrated hydrochloric acid (10 ml.). A little hydrogen sulphide was evolved, the liquid became bright yellow, and yellow plates began to separate, and were collected after 12 hr. at 0°. Crystallisation from ethanol (12 ml. per g.) gave pale yellow leaflets (1·61 g., 55%) of *N*-(thiobenzamido)urea, m. p. and mixed m. p. (with product *a*) 161—162° (decomp.) [Found: C, 49·6; H, 4·7; N, 21·6; S, 16·3%; *M* (cryoscopically, in thymol), 190. Calc. for $C_8H_9N_3OS$: C, 49·2; H, 4·6; N, 21·5; S, 16·4%; *M*, 195].

(*c*) A solution of the urea (0·98 g., 0·005 mole) in water (25 ml.) was refluxed during 30 min., and then concentrated to one-third volume during 15 min. The crystals which had begun to separate during refluxing were collected at 0° (0·58 g., 65%) and consisted of 2-hydroxy-5-phenyl-1,3,4-thiadiazole, m. p. 146—148° (from chloroform–light petroleum) (Found: C, 53·8; H, 3·4. Calc. for $C_8H_6N_2OS$: C, 53·9; H, 3·4%). Lit.,[24] m. p. 146—148°.

N-(*Isopropylideneamino*)*guanidine.*—To the suspension obtained on introducing sodium (1·15 g., 0·05 g.-atom) into anhydrous acetone (50 ml.), finely powdered aminoguanidine sulphate monohydrate (6·6 g., 0·05 mole) was added, and the stirred suspension refluxed during 30 min. The acetone was distilled off in a vacuum, and the residue successively treated with water (25 ml.) [which dissolved all except a few oily droplets] and toluene-*p*-sulphonic acid monohydrate (9·5 g., 0·05 mole) in water (8 ml.). Crystallisation was facilitated by the addition of ethanol (5—10 ml.), and the product collected after 12 hr. at 0° (m. p. 168—170°, after sintering at 164°; 9·3 g., 65%). Crystallisation from ethanol (6 ml. per g., removal of traces of inorganic material under suction; recovery 85%) gave plates of *N*-(*isopropylideneamino*)*guanidine toluene-*p*-sulphonate*, m. p. 172—174° (decomp.) (Found: C, 46·3; H, 6·2; N, 16·2; S, 10·9. $C_4H_{10}N_4,C_7H_8O_3S$ requires C, 46·15; H, 6·3; N, 16·8; S, 11·2%). Addition of an equimolar quantity of 0·05M-aqueous picric acid to an aliquot portion of the original solution gave an orange-yellow precipitate (85%) of the picrate, m. p. 203—206° (decomp.) [from ethanol–water (10 : 1)] (Found: C, 34·8; H, 3·6. Calc. for $C_4H_{10}N_4,C_6H_3N_3O_7$: C, 35·0; H, 3·8%). Finnegan, Henry, and Smith [25] give m. p. 205·5—206·5°.

Attempted thiobenzoylation of the toluene-*p*-sulphonate under the usual conditions gave a deep red solution, from which (thiobenzoylthio)acetic acid was recovered (90%) after 24 hr. at room temperature.

Aromatic Analogues

1-Amino-3-phenylguanidine was prepared by the following modification of the method of Finnegan, Henry, and Lieber.[26] To a solution of *S*-methyl-*N*-phenylthiouronium iodide (29·4 g., 0·1 mole) in water (50 ml.), aqueous 10% hydrazine hydrate (50 ml., 0·1 mole) was added at room temperature, and the resulting two-phase system was stirred during 6 hr. A clear solution was gradually formed, while methanethiol was evolved. The liquid was treated, at 50°, with a solution of silver nitrate (17·0 g., 0·1 mole) in water (30 ml.), any slight excess of silver ions then being removed by dropwise addition of 3N-hydrochloric acid. The silver

[24] Fujii, Yoshikawa, and Yuasa, *J. Pharm. Soc. Japan*, 1954, **74**, 1056; Sato and Ohta, *J. Pharm. Soc. Japan*, 1955, **75**, 1535.

[25] Finnegan, Henry, and Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 2981.

[26] Finnegan, Henry, and Lieber, *J. Org. Chem.*, 1953, **18**, 779; Kirsten and Smith, *J. Amer. Chem. Soc.*, 1936, **58**, 800.

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iodide was filtered off and twice extracted with boiling water (2 × 20 ml.). The combined filtrates were evaporated in a vacuum to approx. 25 ml.; they deposited massive prisms, which were collected at 0° and rinsed with a little ice-water and finally ether [m. p. 119—122° (decomp.), 14·9—16 g., 70—75%]. Crystallisation from ethanol (2 ml. per g.) gave nearly colourless prisms of 1-amino-3-phenylguanidine nitrate, m. p. 120—122° (decomp.) (recovery 90—96%). Finnegan *et al.*[26] give m. p. 121—122°. Interaction of the reactants at 100° resulted in considerable resinification, darkening, and diminished yields.

1-*Amino*-3-p-*tolylguanidine*.—A solution of *S*-methyl-*N*-*p*-tolylthiouronium iodide (15·4 g., 0·05 mole) in water (25 ml.), treated with aqueous 10% hydrazine hydrate (25 ml., 0·05 mole), was stirred at room temperature, until all the methanethiol had volatilised (15 hr.). Treatment with silver nitrate (0·05 mole) as above gave eventually a yellow syrup (approx. 15 ml.) which deposited massive crystals (m. p. 90—94°; 2·3 g., 20%) on prolonged storage at 0° (filtrate: P). Crystallisation from ethanol–ether (10 and 50 ml. per g.) gave prisms of 1-*amino* 3-p-*tolylguanidine nitrate*, m. p. 91—93° (decomp.) (Found: C, 42·35, H, 5·8; N, 31·3. $C_8H_{12}N_4,HNO_3$ requires C, 42·3; H, 5·7; N, 30·8%). Filtrate P (together with the ethanol–ether washing liquids) failed to deposit more product on evaporation and storage. The remaining syrup was dissolved in warm ethanol (10 ml.) and treated with a hot solution of picric acid (9·2 g., 0·04 mole) in ethanol (35 ml.). The product, collected at 0° (10·2 g., 52%), crystallised from ethanol (50 ml. per g.) to yield needles of the *picrate*, m. p. 162—164° (decomp.) (Found: C, 43·1; H, 3·8. $C_8H_{12}N_4,C_6H_3N_3O_7$ requires C, 42·75; H, 3·8%).

1-*Phenyl*-3-(*thiobenzamido*)*guanidine and* 3-*Anilino*-5-*phenyl*-1,2,4-*triazole*.—Solutions of 1-amino-3-phenylguanidine nitrate (6·4 g., 0·03 mole) in water (360 ml.) and 3N-sodium hydroxide (15 ml., 0·045 mole), and of (thiobenzoylthio)acetic acid (6·35 g., 0·03 mole) in water (360 ml.) and 3N-sodium hydroxide (15 ml., 0·045 mole) were mixed and set aside at room temperature during 24 hr. The clear orange-red liquid became turbid suddenly after a few minutes, and a bright yellow granular solid separated gradually. This was collected at 0°, rinsed with water (filtrate G), and carefully air-dried at room temperature (to avoid its conversion into a soft resin) (7—8 g.). The product was dissolved in boiling ethanol (25 ml.), and the filtered liquid gradually diluted with light petroleum (total, 20 ml.). It slowly deposited a crust of yellow crystals (m. p. 171—173°; 2·8—3·6 g., 35—45%) (filtrate F), which gave, after further crystallisation from ethanol–light petroleum (10 and 8 ml. respectively, per g.), pale-yellow granular 1-*phenyl*-3-(*thiobenzamido*)*guanidine*, m. p. 170—172° (decomp.) (Found: C, 62·3; H, 4·6; N, 21·2, 20·3; S, 12·0, 11·5. $C_{14}H_{14}N_4S$ requires C, 62·2; H, 5·2; N, 20·7; S, 11·85%). The product was soluble in sodium hydroxide and reprecipitated by acetic acid.

Filtrate F, on spontaneous evaporation, in two stages (the second with addition of acetone), gave large prisms (0·85—1·05 g., 12—15%). They crystallised from acetone (60 ml. per g., followed by partial evaporation) and afforded prisms of 3-*anilino*-5-*phenyl*-1,2,4-*triazole*, m. p. 220—222° [Found: C, 71·1; H, 5·2; N, 23·9%; *M* (cryoscopically in thymol), 225. $C_{14}H_{12}N_4$ requires C, 71·2; H, 5·1; N, 23·7%, *M*, 236], highly soluble in ethanol–acetone.

The aqueous alkaline filtrate G, on slow spontaneous evaporation to small volume, deposited white solid. Crystallisation from acetone as above gave 3-anilino-5-phenyl-1,2,4-triazole, m. p. 220—222° (0·6 g., 8%).

The *triazole picrate*, obtained quantitatively in ethanol, formed prisms, m. p. 268—270° (decomp.) (from a large volume of ethanol) (Found: C, 52·2; H, 2·8. $C_{14}H_{12}N_4,C_6H_3N_3O_7$ requires C, 51·6; H, 3·2%). The *diacetyl derivative*, obtained nearly quantitatively on refluxing a solution of the triazole (0·002 mole) in acetic anhydride (8 ml.) during 30 min. and stirring the liquid into water, formed prisms, m. p. 200—202° (from acetone–ethanol) (Found: C, 68·1; H, 5·05; N, 17·45. $C_{18}H_{16}N_4O_2$ requires C, 67·5; H, 5·0; N, 17·5%).

When the thiobenzoylation was performed in more concentrated solution, or at higher temperatures, the crude product separated as a yellow sticky resin that crystallised with greater difficulty and was obtained in diminished yield.

1-*Thiobenzamido*-3-p-*tolylguanidine*.—1-Amino-3-*p*-tolylguanidine nitrate (1·135 g., 0·005 mole) was thiobenzoylated as described in the foregoing example. The crude resinous product was ground with water, filtered, dried at room temperature (1·2 g.), and dissolved in ethanol (6 ml.), and the filtered orange solution was diluted with light petroleum (6 ml.). On prolonged storage and partial evaporation the liquid set to a crystalline mass: the collected solid gave, on crystallisation from ethanol–light petroleum (1 : 1 mixture of materials of b. p. 60—80° and 40—60°), white needles (0·54 g., 38%), of 1-*thiobenzamido*-3-p-*tolylguanidine*, m. p. 174—176°

(decomp.) (Found: C, 62·9; H, 5·8; N, 19·8; S, 11·6. $C_{15}H_{16}N_4S$ requires C, 63·4; H, 5·6; N, 19·7; S, 11·3%).

1-*Phenyl*-3-(*thiobenzamido*)*guanidine*.—(a) *Action of hydrochloric acid*. A solution of the reactant (0·54 g., 0·002 mole) in 3N-hydrochloric acid (25 ml.) was refluxed during 10 min. and the resulting liquid, containing a trace of semisolid globules, basified with 3N-sodium hydroxide. The resulting crystalline precipitate (0·48 g.) was collected at 0° and formed prismatic needles (total, 0·4 g., 79%) of 2-anilino-5-phenyl-1,3,4-thiadiazole, m. p. 198—200° (from acetone–ethanol) (Found: C, 66·2; H, 4·2. Calc. for $C_{14}H_{11}N_3S$: C, 66·4; H, 4·35%). Young and Eyre [23] give m. p. 199—200°. The *picrate*, precipitated (90%) when hot saturated ethanolic solutions of the components were mixed, formed prisms, m. p. 202—204° (decomp.) (from a large volume of ethanol) (Found: C, 50·15; H, 3·1. $C_{14}H_{11}N_3S,C_6H_3N_3O_7$ requires C, 49·8; H, 2·9%).

(b) *Action of acetic anhydride*. A solution of the reactant (0·002 mole) in acetic anhydride (8 ml.) was refluxed during 30 min. and then stirred into warm water (50 ml.). The resulting solidified white product (0·42 g.), recrystallised from a large volume of ethanol, yielded needles (0·33 g., 75%) of 2-acetamido-5-phenyl-1,3,4-thiadiazole, m. p. and mixed m. p. (see above) 276—278°.

(c) *Alkali*. The reactant was recovered almost quantitatively after 20 minutes' refluxing in 3N-sodium hydroxide (10% solution).

4-*Phenyl*-1-(*thiobenzoyl*)*semicarbazide*.—(a) *Preparation*. To a stirred solution of (thiobenzoylthio)acetic acid (7·0 g., 0·033 mole) in 0·75N-sodium hydroxide (110 ml., 0·083 mole) at 40°, freshly crystallised, finely powdered 4-phenylsemicarbazide (7·55 g., 0·05 mole) was added; it dissolved rapidly. At room temperature the liquid gradually deposited a granular precipitate, which was collected after 4 hr. (solid S). The filtrate was acidified with 3N-hydrochloric acid (to Congo Red), and gave a copious precipitate, which was collected at 0°, rinsed with water, dried (7 g.), and crystallised from ethanol (40 ml. per g.), platelets of 4-*phenyl*-1-(*thiobenzoyl*)*semicarbazide*, m. p. 188—190° (decomp.), being obtained (5·8—6·7 g., 65—75%) (Found: C, 62·1; H, 5·1; N, 15·6; S, 11·4. $C_{14}H_{13}N_3OS$ requires C, 62·0; H, 4·8; N, 15·5; S, 11·8%).

Solid S (0·6—0·8 g., 15—20%) consisted, after crystallisation from ethanol, of 2,5-diphenyl-1,3,4-thiadiazole, m. p. and mixed m. p. 138—140° (Found: C, 70·3; H, 4·1. Calc. for $C_{14}H_{10}N_2S$: C, 70·6; H, 4·2%).

(b) *Action of hydrochloric acid*. A refluxing solution of the reactant (1·36 g., 0·005 mole) in ethanol (40 ml.) and concentrated hydrochloric acid (8 ml.), which was initially yellow, was decolorised during 3—5 min. Boiling was continued during 15 min., and the liquid then evaporated in a vacuum to small volume (10 ml.) and diluted with water (15 ml.). The crystalline precipitate (0·85 g., 95%) was collected at 0° (filtrate F) and consisted, after crystallisation, of 2-hydroxy 5-phenyl 1,3,4-thiadiazole, m. p. and mixed m. p. (see above) 146—148° (from chloroform–light petroleum).

Filtrate F, treated with 40% aqueous sodium hydroxide (40 ml.) and shaken with benzoyl chloride (5 ml.), gave benzanilide contaminated with ethyl benzoate. The products, isolated by extraction with ether, were separated by removing the solvent and treating the residual mixture with light petroleum (15 ml.). The crystalline solid (0·84 g., 85%) was benzanilide, m. p. and mixed m. p. 162—163° (from ethanol).

(c) *Action of acetic anhydride*. A solution of the reactant (0·005 mole) in acetic anhydride (10 ml.) was refluxed during 20 min. (rapid colour change from deep orange to pale yellow). The solid (m. p. 110—118°; 0·93 g., 85%) obtained on stirring the liquid into warm water (40 ml.), crystallised from ethanol–water (5 : 1), giving 2-acetoxy-5-phenyl-1,3,4-thiadiazole, plates, m. p. 117—119° (Found: C, 54·5; H, 3·5. Calc. for $C_{10}H_8N_2O_2S$: C, 54·5; H, 3·6%). Lawson and Searle [9] give m. p. 117—119°.

(d) *Alkali*. The reactant was recovered almost quantitatively after 20 min. in refluxing 3N-sodium hydroxide (10% solution).

Thiobenzoylation of 4-*Phenyl*-3-*thiosemicarbazide*.—(*a*) The reactant (3·35 g., 0·02 mole), dissolved in water (60 ml.) and 3N-sodium hydroxide (13·3 ml., 0·04 mole) at 40°, was treated with (thiobenzoylthio)acetic acid (4·24 g., 0·02 mole), dissolved in 0·5N-sodium hydroxide (40 ml., 0·02 mole), at the same temperature. The orange liquid was kept at 35° during 0·5 hr., at room temperature during 1 hr., and at 0° during 3 hr.; the whole was then filled with opaque white needles. They were collected at the pump and successively washed with very little ice-water, ethanol–ether, and ether (filtrates: S). The solid (4—5 g.) gave, on crystallisation

from ethanol–ether (10 and 5 ml. per g.), white needles of *sodium 3-mercapto-4,5-diphenyl-1,2,4-triazole trihydrate*, m. p. 151—154° (decomp.) (3·85—4·2 g., 58—64%) (Found: C, 50·8; H, 4·8; N, 12·35; S, 9·5. $C_{14}H_{10}N_3SNa,3H_2O$ requires C, 51·1; H, 4·9; N, 12·8; S, 9·7%). Spontaneous evaporation of the alkaline filtrates S and washing liquids at room temperature (to approx. 50 ml.) resulted once again in a crystalline mass, from which more sodium salt was isolated (up to 1·05 g., 16%). The salt dissolved in water with a strongly alkaline reaction.

(*b*) The solution obtained in the thiobenzoylation [as described in (*a*)] was slowly treated with concentrated hydrochloric acid (30 ml., 0·30 mole). The suspension, which evolved hydrogen sulphide copiously, was boiled during 10 min. and the resulting granular white product collected at 0°. The dried product (5 g.) was dissolved in acetone–ethanol (1 : 1; 300 ml.), and successive crops of solid were obtained by evaporating the liquid in stages. The combined first crops (m. p. 275—282°; 2·5—3·3 g., 50—65%) gave, on crystallisation from acetone–ethanol, needles of 3-mercapto-4,5-diphenyl-1,2,4-triazole, m. p. 280—282° (Found: C, 66·9; H, 4·45; N, 16·65; S, 12·6. Calc. for $C_{14}H_{11}N_3S$: C, 66·4; H, 4·4; N, 16·6; S, 12·65%); Hoggarth [15] gives m. p. 282°. Dissolution of the thiophenol in an equivalent of 0·5N-sodium hydroxide gave the sodium salt trihydrate, m. p. and mixed m. p. 150—152° (decomp.), almost quantitatively.

The final crops (m. p. 190—195°; 1·0—1·8 g., 20—35%) gave, on further crystallisation from acetone–ethanol, pale yellow needles of 2-anilino-5-phenyl-1,3,4-thiadiazole, m. p. and mixed m. p. (see above) 196—198° (Found: C, 66·1; H, 4·6; N, 16·3; S, 12·35. Calc. for $C_{14}H_{11}N_3S$: C, 66·4; H, 4·4; N, 16·6; S, 12·65%).

Nickel Complexes.—An approximately 5% solution of the compound in ethanol was treated dropwise with 5% nickel chloride in 0·3N-hydrochloric acid. The following gave deep-brown solutions: V (R = Ph; *p*-MeC_6H_4); VI (R = Ph). The following did not react: VIII (R′ = Et, Ph·CH_2).

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316. *Studies in Nuclear Magnetic Resonance. Part IV.*[1] *Stereochemistry of the Bixins.*

By M. S. BARBER, A. HARDISSON, L. M. JACKMAN, and B. C. L. WEEDON.

By means of nuclear magnetic resonance, methyl natural bixin is shown to be the *cis*-4-, neomethylbixin A the *cis*-8-, and neomethylbixin C either the *cis*-4,*cis*-8- or the *cis*-4,*cis*-12-isomer.

Natural bixin is shown to have the *cis*-16-structure.

BIXIN (I; R = H) was the first carotenoid in which geometrical isomerism was encountered.[2-6] The common natural isomer of this half-ester, which is the principal pigment in seeds of *Bixa orellana*, gives a higher-melting "stable" form on treatment with catalytic amounts of iodine.[3,4] In an attempt to examine the stereochemical difference between the two forms, Karrer and Solmssen [6] degraded both by carefully controlled permanganate oxidation to apo-1- (II), apo-2- (III), and apo-3-norbixinal methyl ester (IV). The two bixins gave different crystalline apo-1-esters. The apo-2-esters were also thought to be different, but a decision was made difficult by the failure of the products to crystallise except as their derivatives.[7] However, the two bixins were

[1] Part III, Jackman and Wiley, *J.*, 1960, 2886.
[2] Herzig and Faltis, *Annalen*, 1923, **431**, 40.
[3] Karrer, Helfenstein, Widmer, and van Itallie, *Helv. Chim. Acta*, 1929, **12**, 741.
[4] Kuhn and Winterstein, *Ber.*, 1932, **65**, 646; 1933, **66**, 209.
[5] Zechmeister, *Chem. Rev.*, 1944, **34**, 267.
[6] Karrer and Solmssen, *Helv. Chim. Acta*, 1937, **20**, 1396.
[7] Karrer and Jucker, "Carotinoide," Birkhäuser, Basle, 1948.

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reported to give the same apo-3-ester, which was obtained crystalline from some preparations. Karrer and Solmssen, therefore, concluded that the isomeric bixins probably differ in geometrical configuration about the third double bond from the carboxyl group, though in view of the uncertainty about the distinction between the two apo-2-esters the possibility that the second double bond was the site of stereochemical difference could not be entirely excluded.[6,7] (It does not seem to have been considered at this stage that more than one of the first three double bonds might be involved.) Later, visible- and ultraviolet-light absorption studies by Zechmeister and Escue[5,8] on the related diesters (I; R = Me) showed that methyl " stable " bixin had the " all-*trans* "-configuration, and methyl natural bixin * a mono-unhindered *cis*-structure, thus excluding Karrer and Solmssen's *cis*-6-formulation † for bixin A *cis*-4-structure for methyl natural bixin was favoured by Zechmeister and Escue, but subsequent infrared light absorption studies by Lunde and Zechmeister[9] led to the suggestion of a *cis*-2-formulation The " central-*cis* " configuration is excluded by the infrared[9] and other evidence;[10] moreover this isomer has now been synthesised by an unambiguous route and shown to be different from methyl natural bixin.[9,11]

It is obvious that there are as yet no satisfactory answers to the two main problems concerning stereochemistry in the bixin series, *viz.*, (i) the location of the *cis*-bond in methyl natural bixin, and (ii) the position of the *cis*-bond with respect to the free carboxyl group in bixin itself. Previous studies on nuclear magnetic resonance spectroscopy have shown that both chemical shifts and spin–spin coupling constants can afford precise information about the stereochemistry of ethylenic double bonds.[1,12] The solution of the above problems by these means is now reported.‡

The spectra of methyl " all-*trans* "-bixin and methyl natural bixin have many features in common, *viz.*, bands due to the *O*-methyl (τ 6·24) and *C*-methyl protons (8·03), a broad band (near 3·45) in the olefinic-proton region, and a doublet at 4·12 (J 15·8 c./sec.) equivalent to two protons. However, the two spectra differ in the region below 3·0; that of methyl " all-*trans* "-bixin exhibits a doublet at 2·61 (J 15·8) equal in intensity to the doublet at 4·12, whereas that of methyl natural bixin has doublets at 2·63 (J 15·8) and 2·07 (J 15·8) each of which has half the intensity of the doublet at 4·12.

The doublets at 4·12 and 2·61 in the spectrum of methyl " all-*trans* "-bixin clearly arise from two interacting olefinic protons: the relative intensities of the components of the doublets are in good agreement with those calculated from the chemical shift and coupling constant; furthermore, the separation of the components of each doublet is the same at 56·4 as at 40 Mc./sec. The only isolated pairs of mutually interacting protons in methyl " all-*trans* "-bixin are those of the equivalent double bonds at the two ends of the polyene chain. By analogy with many $\alpha\beta$-ethylenic esters[12] the high- and the low-field doublets can be assigned to the protons α and β respectively to the methoxycarbonyl groups, and the observed coupling constant is in good agreement with those of other *trans*-olefins.[13]

The spectrum of methyl natural bixin shows that both the α-protons and one of the β-protons are equivalent to those found in the " all-*trans* "-isomer, whilst the remaining β-proton gives rise to a band which is shifted by 0·56 p.p.m. to lower fields. This shift cannot be associated with a change in stereochemistry of one of the terminal double bonds

* This compound has also been called " natural methylbixin." For the previous nomenclature in the bixin series see refs. 7 and 8.

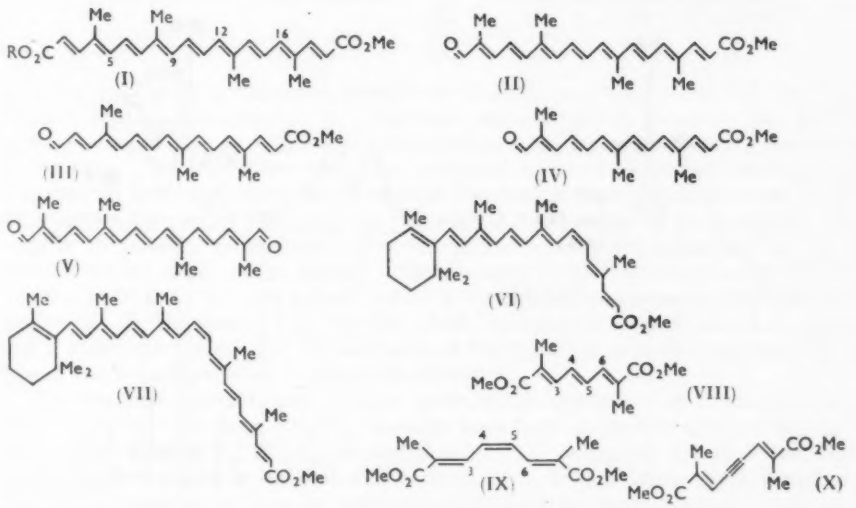
† Geneva numbering; CO_2H in bixin = 1.

‡ A summary of the main results was given in *Proc. Chem. Soc.*, 1960, 23.

[5] Zechmeister and Escue, *J. Amer. Chem. Soc.*, 1944, **66**, 322.
[9] Lunde and Zechmeister, *J. Amer. Chem. Soc.*, 1955, **77**, 1647.
[10] van Hassalt, *Rec. Trav. chim.*, 1911, **30**, 1; 1914, **33**, 192.
[11] Inhoffen and Raspé, *Annalen*, 1955, **592**, 214.
[12] Jackman and Wiley, *J.*, 1960, 2881.
[13] Bishop and Richards, *Mol. Phys.*, 1960, **3**, 114.

because the coupling constants are unaltered and a value of 10—12 c./sec. would have been expected for a *cis*-bond.[13,14] The observed paramagnetic shift can only result from a change in configuration in the immediate neighbourhood of one terminal double bond since the appropriate absorptions of the esters[15] (VI) (4·13, 2·55; $J = 15{\cdot}65$) and (VII) (4·18, 2·60; J 15·6) are virtually identical with those of their " all-*trans* "-isomers (4·19, 2·62, J 15·5; and 4·17, 2·60, J 15·5, respectively). It is therefore necessary to postulate that methyl natural bixin has the *cis*-4-structure, and that the shift is due to the proximity of the β-proton at the *cis*-end of the molecule to the 6,7-double-bond; there is evidence to suggest that the magnetic anisotropy of a carbon–carbon double bond deshields a proton situated close to it in the plane of the bond.[14]

To test the above hypotheses further a pair of model compounds,[16] (VIII) and (IX),



have been examined. In (IX) the β-protons bear the same relation to the 6,7-double bond as that just postulated for one of the β-protons in methyl natural bixin. An analysis (see below) of the complex region of the spectra of (VIII) and (IX) shows that the absorption due to the β-protons in the *cis*-isomer (IX) is shifted (0·58 p.p.m.) in a similar manner to that observed with one of the β-protons in methyl natural bixin. There is therefore no doubt that methyl natural bixin has the *cis*-4-structure.

By thermal or photochemical stereomutation of methyl " all-*trans* "-bixin and methyl natural bixin, Zechmeister and Escue[8] obtained two other crystalline isomers, neo A and neo C respectively, as the principal products. Light-absorption studies revealed that neo A also has a mono-unhindered *cis*-structure.[8,9] A strong " *cis*-peak " indicated that the *cis*-bond is near the centre of the molecule. Since neo A differs both from methyl natural bixin and from the synthetic " central-*cis* " -isomer,[9] it must have the *cis*-8-structure. The visible-light absorption properties of neo C are those of an isomer with two unhindered *cis*-bonds, and the infrared spectrum indicates the absence of a central *cis*-bond.[5,9] In the nuclear magnetic resonance spectrum the band pattern due to the α- and β-protons (4·13, 2·60, 2·03) is very similar to that observed with methyl natural bixin. Neo C must

[14] Jackman, " Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, London, 1959, p. 129.
[15] Isler, Guex, Rüegg, Ryser, Saucy, Schwieter, Walter, and Winterstein, *Helv. Chim. Acta*, 1959, **42**, 864.
[16] Mildner and Weedon, *J.*, 1953, 3294.

therefore be either the *cis*-4,*cis*-8- or the *cis*-4,*cis*-12-isomer, probably the latter since neo C is formed under conditions which convert methyl " all-*trans* "-bixin into the neo A isomer.

In an approach to the second main problem, the insolubility of the bixins in common solvents precluded direct comparison of their nuclear magnetic resonance spectra. A search for more suitable solvents was not undertaken because it was expected that the

FIG. 1.* *The observed and theoretical spectra at 40 Mc./sec. of methyl " all-*trans *" - 2,7 - dimethylocta - 2,4,6-trienoate* (VIII). *Lines 6 and 11 of the B half-spectrum overlap the A half-spectrum. The band a arises from transitions of the A nuclei.*

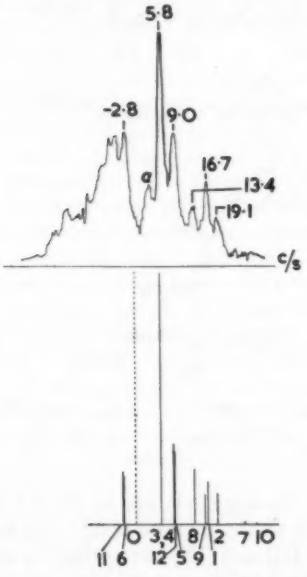
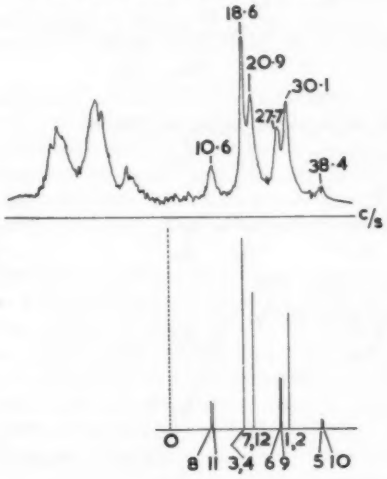


FIG. 2.* *The observed and theoretical spectra at 40 Mc./sec. of methyl* 2,7-dimethylocta-trans-2,cis-4,trans-6-*trienoate* (IX).



* The line numbering used is that of Pople, Schneider, and Bernstein.[17]

shielding contributions of the carboxy- and methoxycarbonyl groups would be so similar that no unambiguous assignment of the bands would be possible. Attention was therefore directed to the *cis*-apo-1-norbixinal methyl ester (II) described by Karrer and Solmssen;[6] a preliminary examination of crocetindial (V) revealed that the band due to the proton β to the aldehyde group in (II) would not be resolved from the broad band near 3·45. The spectrum of the *cis*-apo-1-ester in the olefinic proton region showed only two doublets (4·08, *J* 15·8; 2·04, *J* 15·8), each equivalent to one proton. Since these are clearly characteristic of the *cis*-end of methyl natural bixin, the *cis*-bond in natural bixin itself must be assigned to the 16-position in the esterified half of the molecule. This conclusion is not necessarily at variance with the degradative results of Karrer and Solmssen. Although it was stated that both natural and " all-*trans* "-bixin yielded the same apo-3-nor bixinal methyl ester (IV), the only experimental details given of the isolation of the latter from a compound of the *cis*-series relate to the oxidation of *methyl* natural bixin in

[17] Pople, Schneider, and Bernstein, " High-resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959, p. 139.

which the position of attack is ambiguous. The only evidence given for the formation of apo-3-norbixinal methyl ester from natural bixin was the visible-light absorption maxima of a chromatographic fraction.

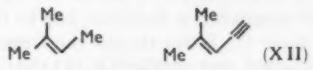
The analysis of the spectra of the two model esters (VIII) and (IX) requires comment. In both esters the protons of the terminal *C*-methyl groups are coupled to the adjacent olefinic protons and the spectra therefore depart from the four-spin system, A_2B_2. However, in both cases, the high-field band (see Figure) is little affected by the small interactions involving the methyl groups, and can therefore be analysed as an A_2B_2 system in which the positions of the lines yield explicitly the chemical shift and the four coupling

Chemical shifts (c./sec.) *and coupling constants* (c./sec.) *at* 40 Mc./sec. *for the olefinic protons in the triene esters* (VIII) *and* (IX).

		J_{34}	J_{35}	J_{36}	J_{45}
(VIII)	20·0	11·5	−0·6	±0·3	14·6
(IX)	47·1	12·5	−1·0	±0·2	10·7

constants.* The computations involved in the analysis were carried out with the English Electric DEUCE Computor. A programme was contructed in which line positions corresponding to various assignments of the half spectra (run at 40 Mc./sec.) were read in as raw data. The parameters were then computed and used to evaluate the eigenvalues and eigenvectors from which the theoretical line positions and intensities were derived; these were subsequently punched. In this way, it was possible to check rapidly a large number of possible assignments. The theoretical spectra corresponding to the best assignments are shown in the Figures. The spectrum of the " all-*trans* "-ester (VIII) was also run at 56·4 Mc./sec. and agreed well with the theoretical spectrum computed for this frequency. In the spectrum at 56·4 the bands arising from pairs of lines 6,11 of the A and B half-spectra overlap at the mid-point of the spectrum, and the band from the pair 7,10 of the B half-spectrum is clearly observable.

The coupling constants and chemical shifts of the two triene esters are given in the annexed Table. The large coupling constants have been assumed to have positive values. The relative signs of J_{34} and J_{35} are significant. The spectra did not allow the relative signs of J_{36} and J_{45} to be decided, and in any case J_{36} is zero within experimental error. The values obtained for J_{45} in the two compounds prove the stereochemistry of the central double bonds to be that previously assigned from a consideration of the mode of preparation of the two isomers, and supported by their infrared absorptions. That the configuration of the two remaining double bonds is as shown in the formulæ can be justified as follows. The low-field bands in the spectra of the triene esters must be assigned to the protons at $C_{(3)}$ and $C_{(6)}$ because of the observable broadening caused by coupling with the methyl protons. If the terminal double bonds had the opposite configuration to that shown the protons at $C_{(4)}$ and $C_{(5)}$ would have been found at the lower field; studies on the three isomeric dimethyl muconates show that a methoxycarbonyl group deshields a *cis*-γ-proton more efficiently than a *cis*-β-proton.[19] Further, the two olefinic protons of the acetylenic



(XI) (XII)

precursor (X) of the triene esters absorb at 3·19 which is almost identical with the position of absorption of the olefinic proton in methyl tiglate (τ 3·27; cf. methyl angelate, τ 4·02).[1] The presence of the acetylenic group does not invalidate this comparison since the olefinic protons in 2-methylbut-2-ene (XI)[12] and 4-methylpent-3-en-1-yne (XII) absorb at 4·79 and 4·83 respectively.

* The parameter $K = J_A + J_B$[17] can be expressed explicitly in terms of line positions by taking advantage of the diagonal sum rule.[18]

[18] Condon and Shortley, " The Theory of Atomic Spectra," Cambridge University Press, 1953, p. 19.
[19] Jackman and Elvidge, *Proc. Chem. Soc.*, 1959, 89.

Experimental

Nuclear Magnetic Resonance Spectroscopy.—All spectral measurements were made on *ca.* 5% solutions in deuterochloroform at 21° by using a Varian Associates spectrometer (40 and 56·4 Mc./sec.). Tetramethylsilane was employed as an internal reference and the spectra were calibrated by the side-band technique with a Muirhead decade oscillator. The precision of most measurements was ±0·025 p.p.m. The accuracy of measurements on the triene esters (Table) was ±0·3 c./sec.

Methyl 2,7-Dimethylocta-2,4,6-trienoate.—The *trans,cis,trans-* (IX) and " all-*trans* "-isomer (VIII) were prepared by the method of Mildner and Weedon.[16] The *cis*-isomer had $\nu_{max.}$ (in $CHCl_3$) 1701 (CO_2Me) and 1608 cm.$^{-1}$ (C=C stretch). The " all-*trans* "-isomer had $\nu_{max.}$ (in $CHCl_3$) 1696 (CO_2Me), 1620 (C=C stretch), and 974 cm.$^{-1}$ (*trans*-–CH=CH–, out-of-plane C–H deformation).

cis-*Apo*-1-*norbixinal Methyl Ester* (IV).—Oxidation of natural bixin (207 mg.) by the method of Karrer and Solmssen,[6] chromatography of the crude product on alumina (Grade IV) from benzene, and crystallisation from methanol, gave the *cis*-apo-1-ester (15 mg.), m. p. 148—149° (evacuated capillary, uncorr.), $\lambda_{max.}$ (in C_6H_6) 456 and 485 mμ (10^{-3} ε 93·4 and 83·5 respectively), $\nu_{max.}$ 1697 and 1664 cm.$^{-1}$ (ε 410 and 940, conjugated CO_2Me and conjugated CHO, respectively), τ (determined at 40 Mc./sec.) 8·00 with an inflexion at 8·10 (*C*-Me), 6·20 (CO_2Me) and 0·50 (CHO), with the expected relative intensities (for bands due to olefinic protons, see text). Karrer and Solmssen [6] give m. p. 156°, $\lambda_{max.}$ (in light petroleum), 441 and 470 mμ.

Neomethylbixin C.—The method of Zechmeister and Escue [8] was modified in the following way. A solution of methyl natural bixin (200 mg.) in hot benzene (100 ml.) was boiled under reflux for 1 hr., evaporated (to 10 ml.) under reduced pressure, and cooled. The methyl natural bixin (110 mg.) which crystallised was collected and treated as above; the recovered methyl natural bixin (55 mg.) was again recycled. The combined mother-liquors were evaporated (to 5 ml.). Repeated chromatography on alumina (Grade IV) from benzene and finally collection of the lower yellow band, evaporation, and crystallisation from benzene–methanol gave neomethylbixin C (15 mg.), m. p. 155°, $\lambda_{max.}$ 440, 465, and 498 mμ, $\nu_{max.}$ 1691 cm.$^{-1}$ (ε = 880), τ (determined at 56·4 Mc./sec.) 8·02 (*C*-Me) and 6·23 (CO_2Me) with the expected relative intensities (for bands due to olefinic protons, see text). Zechmeister and Escue [8] give m. p. 150—151°.

4-*Methylpent*-3-*en*-1-*yne* (XII) (with P. E. Schwed).—Phosphorus oxychloride (10 ml.) in pyridine (20 ml.) was added in 30 min. to a stirred solution of 2-methylpent-4-yn-2-ol [20] (8·0 g.) in pyridine (20 ml.) at 0°. The mixture was stirred at 20° for 30 min. and then poured on concentrated hydrochloric acid (30 ml.) and ice. The upper hydrocarbon layer was separated, washed with water, dried (Na_2SO_4), and distilled, giving the acetylene (2·0 g., 30%), b. p. 71—74°/760 mm., n_D^{21} 1·4336, $\lambda_{max.}$ (in EtOH) 225 mμ ($E_{1\,cm.}^{1\%}$ 780), which was shown by gas–liquid chromatography to contain small amounts of impurities. Conversion into the *mercury derivative*, which crystallised from alcohol and had m. p. 162° (Found: C, 40·25; H, 4·2. $C_{12}H_{14}Hg$ requires C, 40·25; H, 3·9%), and regeneration with 30% aqueous cyanide at 60—70°, gave 4-methylpent-3-en-1-yne, b. p. 72—73°/760 mm., n_D^{21} 1·4340, $\lambda_{max.}$ (in EtOH) 225 mμ (ε 8600), $\nu_{max.}$ 3268 and 2105 cm.$^{-1}$ (C≡CH), τ (determined at 40 Mc./sec.) 8·26, 8·21 (*C*-Me), 7·32 (conjugated C≡CH), and 4·83 (olefinic proton). Mondon [21] gives b. p. 73—75°.

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Department of Chemistry, Imperial College of Science and Technology,
South Kensington, London, S.W.7. [*Received, October 18th*, 1960.]

[20] Henbest, Jones, and Walls, *J.*, 1949, 2696.
[21] Mondon, *Annalen*, 1952, **577**, 181.

317. *The Molecular Structure of Some Products from the Ehrlich–Sachs Reaction.*

By D. M. W. Anderson and J. L. Duncan.

Several families of compounds, obtained as products of Ehrlich–Sachs-type reactions (reactive methylene compounds and aromatic nitroso-compounds), have been studied in solution by infrared spectroscopy. Deductions regarding the molecular structure of these compounds have been made. Several absorptions which occur at abnormal infrared frequencies are discussed.

The Ehrlich–Sachs reaction, *i.e.*, the base-catalysed condensation of a reactive methylene compound with an aromatic nitroso-compound, has been the subject of recent investigations,[1,2] and the characteristic absorptions in the infrared spectra (obtained for mulls) of typical series of Ehrlich–Sachs products have been reported.[2]

(I) *p*-$NMe_2 \cdot C_6H_4 \cdot N{:}C(CN) \cdot CO_2Et$ *p*-$Me \cdot NH \cdot C_6H_4 \cdot N{:}C(CN) \cdot CO_2Me$ (II)

In some of the series, striking variations in the absorptions given by homologous compounds were observed. Thus *N*-(α-cyano-α-ethoxycarbonylmethylene)-*N'N'*-dimethyl-*p*-phenylenediamine (I) gave a carbonyl absorption at 1740 cm.$^{-1}$, whereas its methoxy-analogue absorbed at 1708 cm.$^{-1}$. Moreover, *N*-(α-cyano-α-methoxycarbonylmethylene)-*N'*-methyl-*p*-phenylenediamine (II) existed in three crystalline modifications, (*a*) maroon needles, m. p. 170° (from methanol), $\nu_{C:O}$ 1687 cm.$^{-1}$, (*b*) yellow-orange needles, m. p. 170° (from benzene), $\nu_{C:O}$ 1713 cm.$^{-1}$, and (*c*) dark red prisms with blue fract, m. p. 168° (from the benzene mother-liquor), $\nu_{C:O}$ 1733 and 1706 cm.$^{-1}$.

These and certain other features of the spectra obtained indicated that the compounds merited further examination. Analytical specimens of the various series of compounds were kindly placed at our disposal for this purpose by Professor F. Bell, who has described their method of preparation.[1,2]

Experimental.—A Hilger H800 spectrophotometer fitted with a sodium chloride prism was used. Calibration was effected with reference to pyrrole vapour (3530 cm.$^{-1}$), polystyrene film (3029 and 2923 cm.$^{-1}$), dichloroacetonitrile (2261 cm.$^{-1}$), and acetone vapours (1742 cm.$^{-1}$), and is believed to be accurate to ±10 cm.$^{-1}$ in the N–H_{st} absorption region, ±5 cm.$^{-1}$ in the C:N absorption region, and ±2 cm.$^{-1}$ for carbonyl absorptions. Solutions in carbon tetrachloride or in chloroform (0·005—0·02M) were examined in a matched pair of variable-path-length cells fitted with sodium chloride windows. Solvent absorptions were removed by compensation in the reference beam. Absorptions are quoted as cm.$^{-1}$.

Ehrlich–Sachs Dinitriles.—Table 1 gives the cyano-absorption frequencies of *N*-dicyanomethylene-*N'N'*-dialkyl-*p*-phenylenediamines as solids and as 0·01M-solutions in chloroform. (Certain of the mull absorptions previously given [2] are corrected.)

Table 1. *Cyano-absorptions of* 4,2,1-$RR'N \cdot C_6H_3R'' \cdot N{:}C(CN)_2$.

R	R′	R″	C:N (mull)	C:N (solution)
Me	Me	H	2216, 2197	2227, 2212sh
Me	Et	H	2212, 2202sh	2224, 2211sh
Et	Et	H	2213 (1 peak only)	2223, 2209sh
Me	Me	Me	2214, 2198	2221, 2210sh
Et	Et	Me	2214, 2198	2223, 2210sh

Space-filling models of these molecules show that the two cyano-groups exist in markedly different environments, as illustrated by (III), the least steric hindrance being given when

[1] Bell, *J.*, 1957, 516.
[2] Anderson and Bell, *J.*, 1959, 3708.

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the $-N{:}C(CN)_2$ group is perpendicular to the plane of the benzene ring. The cyano-group lying in close proximity to the benzene ring will be subject to interaction with the π-electron cloud. Despite non-planarity of the molecule, the cyano-group remote from the benzene ring can be conjugated to the latter by interaction of the ring π-cloud, N atom lone-pair, $N{:}C$ π-cloud and $C{:}N$ π-cloud. It is therefore proposed that the cyano-group remote from the benzene ring absorbs at 2210 ± 2 cm.$^{-1}$, the cyano-group in close proximity to the ring absorbing at 2224 ± 3 cm.$^{-1}$. The validity of these deductions is supported by the behaviour in solution of the Ehrlich–Sachs esters discussed below.

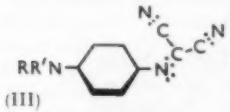

(III)

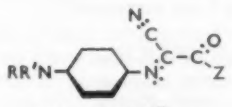
Table 1 shows that the presence of a methyl group in the 2-position of the ring (R″ in Table 1) does not alter the absorption frequency of either cyano-group, although greater steric hindrance to free rotation is created. A study of models, however, shows that the configuration which departs least from planarity and so has the greatest stability is given when the cyano-group and the hydrogen atom in the 6-position are in close proximity. The preferred molecular configuration will, therefore, not be changed by introduction of a methyl group into the 2-position. This effect also applies to the other series of compounds discussed in this paper.

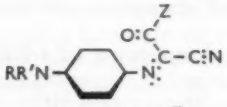
Ehrlich–Sachs Esters.—Table 2 lists the cyano and carbonyl absorption frequencies of *N*-(α-cyano-α-alkoxycarbonylmethylene)-*N′N′*-dialkyl-*p*-phenylenediamines (R′ = Me, Et) and of *N*-(α-cyano-α-alkoxycarbonylmethylene)-*N′*-alkyl-*p*-phenylenediamines (R′ = H) as mulls and as 0·005M-solutions in carbon tetrachloride.

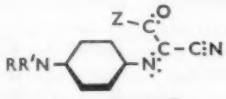
TABLE 2. *Cyano- and carbonyl absorption of* $4,2,1\text{-RR′N·C}_6\text{H}_3\text{R″·N:C(CN)·CO}_2\text{R‴}$.

				C:N		C:O	
				Mull	Soln.	Mull	Soln.
Me	Me	H	Me	2220	2212	1708	1757, 1731
Me	Me	H	Et	2200	2213	1740	1754, 1724
Et	Et	Me	Et	2200	2207	1694	1750, 1722
Et	H	H	Et	orange 2220 maroon 2202	2211	1750 1726	1756, 1726
Me	H	H	Me	orange 2210 maroon 2198	2216	1713 1687	1760, 1733
Et	H	H	Me	2210	2214	1731	1760, 1733
Me	H	H	Et	2215	2216	1741	1756, 1727

The marked variations in both the carbonyl and the cyano-absorption frequencies given by mulls disappear when the compounds are studied in solution, which give two carbonyl bands. The low and constant single absorption (2211 ± 5 cm.$^{-1}$) of the cyano-group indicates, in terms of the deduction already made concerning cyano-groups, that


(IV) Z = OR″
(IX) Z = NH_2


(V) Z = OR″
(VII) Z = NH_2


(VI) Z = OR″
(VIII) Z = NH_2

of the two possible geometrical isomers (IV) and (V) the latter is preferentially formed under the reaction conditions used.[1]

The occurrence of a single C:O frequency in the solids and of two in the solutions is clear evidence that the molecules can exist as rotational isomers, as represented by (V) and (VI).

Models show that whilst rotation can take place about the C–CO_2R''' bond, no free rotation is possible about the N–ring bond. In (V), the carbonyl group is in close proximity to the π-cloud of the benzene ring, and the resulting interaction will raise the carbonyl frequency. (An α-activated αβ-unsaturated ester would be expected [3] to give absorption in the range 1735—1750 cm.$^{-1}$.) In (VI), the OR''' group is in close proximity to the π-cloud of the benzene ring. This will result in an increased contribution from the $R'''O^+{:}C{-}O^-$ polar canonical form to the carbonyl absorption. This resonance form may be further stabilised by interaction of the opposed formal charges on the carbonyl-oxygen atom and the closely adjacent carbon atom of the cyano-group. Thus the carbonyl frequency of isomer (VI) should be considerably lower than that of (V); the assignments of 1755 ± 5 and 1725 ± 5 cm.$^{-1}$ can be made to (V) and (VI) respectively.

Temperature-dependence measurements were made to investigate the relative stabilities of the two isomers (V) and (VI) for each member of the series. In every case the intensity of absorption of the 1725 cm.$^{-1}$ band increased with temperature. Isomer (VI) is therefore the less stable form.[4] The fact that the more stable form is that in which the opposition of like charges is greater has been previously discussed,[4] but is apparently not yet fully understood.

The variations in the carbonyl absorptions of the solids can be attributed to the fixation of one or other isomer, consistent with the production of the lattice of lowest energy. Two of the compounds studied (see Table 2) were isolated in two crystal forms. Use of a Kofler hot-stage microscope showed that in each case one of the forms was unstable, having a transition temperature below the true melting point at which it irreversibly changed, accompanied by a change in colour and crystal structure, to the more stable crystallographic form. Thus the maroon form of *N*-(α-cyanoethoxycarbonylmethylene)-*N'*-ethyl-*p*-phenylenediamine changed at 86° to the orange form (m. p. 107°); for *N*-(α-cyanomethoxycarbonylmethylene)-*N'*-methyl-*p*-phenylenediamine the orange form changed at 158° to the maroon form (m. p. 170°). Infrared studies of the temperature-dependence of these two compounds showed that, at the transition temperature, two carbonyl absorptions were given, one of which slowly decreased in intensity as the temperature was gradually raised, finally leaving the other as a single band. When the compound eventually melted, the two bands reappeared.

These examples of rotational isomerism support the initial assignments to the cyano-frequencies in Ehrlich–Sachs dinitriles: if the assignments be reversed, leading to (IV) in place of (V), models show that, although rotational isomerism of the ester group is still possible, an explanation of the large differences in the two carbonyl absorptions can no longer be found.

Ehrlich–Sachs Amides.—0·01M-Solutions in chloroform of several *N*-carbamoylcyanomethylene-*N'N'*-dialkyl-*p*-phenylenediamines all showed a cyano-band at 2211 ± 3 cm.$^{-1}$. The assignment for cyano-groups therefore favours the structure (VII), or its possible rotational isomer (VIII), rather than (IX). In the carbonyl absorption region, bands were present at 1694 ± 2 (s), 1618 ± 1 (s), and at 1555 (w) and 1495 (s). When each compound was studied in a range of solvents of varying polarity,[5] the 1694 cm.$^{-1}$ band varied between 1710 cm.$^{-1}$ (CCl_4) and 1691 cm.$^{-1}$ ($CHBr_3$), whilst the other three bands remained constant. A $d\nu/\nu$ plot (based on carbon tetrachloride) for the 1691—1710 cm.$^{-1}$ band against acetophenone [5] gave a straight line. Hence only one carbonyl band is given in solution, the 1618 cm.$^{-1}$ band being attributed to the N:C bond. Rotational isomerism, although feasible on steric grounds, is therefore not exhibited by these amides.

It is well known that the contribution of the polar canonical form $H_2N^+{:}C{-}O^-$ in amides is considerable, and is responsible [3] for occurrence of the carbonyl absorption normally

[3] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., London, 1958, 2nd edn., pp. 179, 205.
[4] Bellamy, Thomas, and Williams, *J.*, 1956, 3704.
[5] Bellamy and Rogasch, *Spectrochim. Acta*, 1960, **16**, 30.

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near 1690 cm.$^{-1}$ for dilute solutions. An α-activated αβ-unsaturated amide would also be expected to give a carbonyl band near 1690 cm.$^{-1}$. The observed 1691—1710 cm.$^{-1}$ band, therefore, indicates that an activation effect on the carbonyl group is tending to reduce the $H_2N^+{:}C{-}O^-$ contribution: this effect would be given in structure (VII), on the basis of the reasoning in the discussion of Ehrlich–Sachs esters. Structure (VIII) would involve increased contribution by the form $H_2N^+{:}C{-}O^-$, leading to an absorption frequency much lower than that normally exhibited by amides. It is concluded that in structure (IX) the charge-distribution effects become so great that this isomer is unstable.

The compound *N*-carbamoylcyanomethylene-*N'N'*-di-n-propyl-*p*-phenylenediamine [1] was, however, found to give two carbonyl bands at 1714w and 1657s cm.$^{-1}$ in the solid state. For the liquid state and for chloroform solution only one band at 1694 cm.$^{-1}$ was given. Repeated purification failed to yield material in which the 1714 cm.$^{-1}$ band was absent from the solid-state spectrum. Identical spectra were given by crystals grown from different solvents and from cast films: the possibility of the presence of dimorphic crystal forms is therefore small. The cause of this effect was not determined. A similar crystal effect was given by *N*-(α-cyano-α-methoxycarbonylmethylene)-*N'*-methyl-*p*-phenylenediamine (II) (see Table 2); on one occasion a third isomer, strongly crystalline and giving absorptions at 1733m and 1706m cm.$^{-1}$, was obtained. On melting, the compound crystallised as the stable yellow-orange isomer, giving absorption at 1713 cm.$^{-1}$. Numerous recrystallisation attempts failed to yield any further quantity of the third isomer, which would appear to have been formed by the simultaneous crystallisation of both rotational isomers.

Condensations involving 2 Mols. of Cyanoacetic Esters and Condensations between Dinitriles and Esters.—These respectively produce *N*-(2-cyano-1,2-dialkoxycarbonylvinyl)-*N'N'*-dialkyl-*p*-phenylenediamines and *N*-(1,2-dicyano-2-alkoxycarbonylvinyl)-*N'N'*-dialkyl-*p*-phenylenediamines [2] (see Table 3a and b respectively). It was suggested [2] on infrared evidence that these contained an N–H group; this has now been confirmed by alkaline hydrolysis to the corresponding *NN*-dialkyl-*p*-phenylenediamines, which were characterised as their acetyl and benzoyl derivatives.[6]

When both series of compounds were studied as mulls, their characteristic NH, CN, and CO frequencies were little influenced by the nature of the alkyl groups. For each series, the variation between compounds is shown in Table 3.

Each compound in the two series was then studied in solution (0·01M) in each of the following solvents: carbon tetrachloride, methylene chloride, chloroform, diethyl ether,

TABLE 3. *Solid and solution spectra:* (a) 4,2,1-RR'N·C_6H_3R''·NH·C(CO_2R''')$:$C(CN)·CO_2R''', (b) 4,2,1-RR'N·C_6H_3R''·NH·C(CN)$:$C(CN)·CO_2R'''

	N–H			C$:$N		C$:$O					
	Mull *	Soln.*	Solvent † vartn.	Mull *	Soln.*	Mull *	Soln.*	Solvent † vartn.	Mull *	Soln.*	Solvent † vartn.
(a)	3275 ±20	3215 ±10	±5	2228 ±8	2222 ±5	1755 ±5	1755 ±5	±7	1675 ±5	1675 ±5	±2
(b)	3235 ±35	3220 ±20	±10	2222 ±12 (1 peak only)	2220 ±5	—	—	—	1688 ±6	1678 ±6	±3

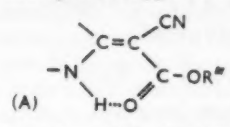
* ±x = limits of variation between compounds in the series.
† Max. frequency shift of any compound when examined in solvents of differing polarities.

nitromethane, and bromoform. The NH and CO frequencies of each varied little with change of solvent; Table 3 shows the maximum frequency shift given by any of the compounds of each series.

In these compounds, the low frequencies of the N–H absorption and of a carbonyl

[6] McKusick, Heckert, Cairns, Coffman, and Mower, *J. Amer. Chem. Soc.*, 1958, **80**, 2806.

absorption suggest the existence of strong intramolecular hydrogen bonding. Models show that group (A) (inset) forms a compact six-membered ring system; the frequency 1675 cm.$^{-1}$ is therefore assigned to this ester group. The variation of this band in different solvents is small, ± 3 cm.$^{-1}$ (Table 3); this is consistent with strong intramolecular hydrogen bonding, which prevents normal interaction of proton-donating solvents with the C:O link.[7] The second ester group (1755 cm.$^{-1}$) in series (a) (Table 3) suffers severe steric hindrance and is almost 90° out of plane with respect to the C:C bond. The absorption frequency observed is therefore more typical of a saturated ester than of an αβ-unsaturated ester (cf. ref. 8).



(A)

The Colour of N-(2-*Alkoxycarbonyl*-1,2-*dicyanovinyl*)-N′N′-*dialkyl*-p-*phenylenediamine*.—These compounds lack extended conjugation but are dark red. Solutions in chloroform showed a broad band with $\lambda_{max.}$ 453 mμ. A study of very dilute solutions (5×10^{-4} to 5×10^{-5}M) in chloroform in 1—10 mm. quartz cells showed that the intensity of the 453 mμ band decreased rapidly with decreasing concentration, whilst a new band ($\lambda_{max.}$ 346 mμ) increased in intensity. The spectra exhibited an isosbestic point at 394 mμ; two species were therefore present in solution.

To investigate this effect, a series of tricyanovinylanilines, $R{\cdot}C_6H_4{\cdot}NH{\cdot}C(CN){:}C(CN)_2$, was prepared,[6] where R = H, Me, Et, Pr^i, Bu^t, OMe, and NMe_2. The series therefore had increasing electron-donation from the R groups in the *para*-position. The series ranged in colour from pale yellow for R = H to orange for R = OMe, but the R = NMe_2 compound was deep maroon. The yellow series had $\lambda_{max.}$ ranging from 348 mμ for R = H to 362 mμ for R = OMe (5×10^{-4}M-solutions in chloroform); this absorption is clearly due to the simple molecule. For *p*-*NN*-dimethyltricyanovinylaniline, however, the visible band (445 mμ) decreased with decreasing concentration in very dilute solutions (5×10^{-4} to 5×10^{-6}M in chloroform) whilst a band at 370 mμ simultaneously increased. An isosbestic point occurred at 403 mμ.

The anomalous deep colour of *p*-*NN*-dimethyltricyanovinylaniline and of the series of *N*-(2-alkoxycarbonyl-1,2-dicyanovinyl)-*N′N′*-dialkyl-*p*-phenylenediamines may therefore be attributed to some form of self-π-complexing arising from the particular molecular structure. The complex is destroyed at very high dilutions, with liberation of the simple molecules which absorb in the expected ultraviolet region.

The authors thank the Carnegie Trust for a Scholarship (to J. L. D.), and Drs. L. J. Bellamy and J. C. P. Schwarz for helpful discussions. They are indebted to Dr. B. C. McKusick for a generous gift of tetracyanoethylene, and to Professor F. Bell for kindly providing samples for investigation and for his interest in this work.

Department of Chemistry, University of Edinburgh. [*Received, July 29th*, 1960.]

[7] Bellamy and Hallam, *Trans. Faraday Soc.*, 1959, **55**, 220; Bellamy and Rogasch, *J.*, 1960, 2218.
[8] Felton and Orr, *J.*, 1955, 2170.

318. *The Reactions of Organic Phosphates. Part IV.* Oxygen Exchange between Water and Orthophosphoric Acid.*

By C. A. Bunton, D. R. Llewellyn, C. A. Vernon, and V. A. Welch.

The rates of oxygen exchange of inorganic orthophosphate have been measured over a wide range of pH. A plot of exchange rate against pH has a maximum at pH *ca.* 5 and a minimum at pH *ca.* 1; the curve steepens rapidly with increasing hydrogen-ion concentration. This pH dependence is very similar to that observed for the hydrolysis of methyl dihydrogen phosphate. The mechanisms of the two processes are very similar and we compare their rates.

Potassium dihydrogen orthophosphate slowly exchanges its oxygen atoms with water by a reaction which does not involve formation and hydrolysis of higher phosphates.[1] There have been several qualitative investigations of the oxygen exchange of inorganic phosphates,[1,2] but the only kinetic study has been on concentrated solutions of orthophosphoric acid.[3] In this special system it seems that condensed phosphoric acids are intermediates.

The work now described has been with dilute solutions of phosphate, and shows that the oxygen exchange of orthophosphoric acid, and its anions, proceeds by mechanisms which are analogous to those which give phosphorus–oxygen bond fission in the hydrolysis of monoalkyl phosphates. These hydrolytic mechanisms are now well characterised, and the main reactive species are the conjugate acid and the monoanion of the ester.[4,5] Preliminary accounts of our exchange results have been given elsewhere.[6]

The variation, with acidity, of the first-order rate constant, k_E, for the oxygen exchange of orthophosphoric acid, is shown in Figs. 1 and 2. The forms of the plots are very similar to those observed for the hydrolyses of the monoesters.[4,5]

Oxygen Exchange at pH 1—9.—The kinetics of the oxygen exchange in this pH range (Fig. 1) can be analysed by the procedures applied to the hydrolyses of monoalkyl phosphates.[5] The rate of exchange has a maximum value at pH 4·5—5·5, where the monoanion, $H_2PO_4^-$, is the predominant species. Thus we conclude that, as for the ester hydrolysis, reaction is by attack of water upon the monoanion (other possible mechanisms can be excluded for reasons given elsewhere [4,5]). The value of the rate at pH *ca.* 5 gives us an approximate value for the rate coefficient, k_M, for the reaction between the monoanion and water. A more exact value can be obtained by correction for the small amount of exchange which comes from reaction between the undissociated acid, H_3PO_4, and water. The first-order rate constant, k_N, for this exchange can be estimated by two methods.

(*a*) The plot of k_E against the hydrogen-ion concentration can be extrapolated to zero acidity. This gives a value of $10^6k_N \approx 1{\cdot}3$ sec.$^{-1}$. (*b*) From the rates of exchange at two different pH's, 2·21 and 4·00, and the relative amounts of H_3PO_4 and $H_2PO_4^-$ at these pH's, we can calculate $10^6k_M = 4{\cdot}03$ sec.$^{-1}$, and $10^6k_N = 1{\cdot}28$ sec.$^{-1}$. The values of k_N agree well and, as a further test of our method, we have calculated the extents of exchange by reaction of H_3PO_4 and $H_2PO_4^-$. These are plotted in Fig. 1 (broken lines). The full line is their sum, together with the contribution of the acid-catalysed exchange which becomes significant only below pH 0·5.†

* Part III, *J.*, 1960, 3293.

† Dissociation constants and pH values were measured at 20°. The error involved in using these data to interpret the kinetic results, obtained at 100°, appears to be small.

[1] Winter and Briscoe, *J.*, 1942, 631.
[2] Brodskii and Sulima, *Doklady Akad. Nauk S.S.S.R.*, 1953, **92**, 589; *Chem. Abs.*, 1954, **48**, 5620.
[3] Keisch, Kennedy, and Wahl, *J. Amer. Chem. Soc.*, 1958, **80**, 4778.
[4] Butcher and Westheimer, *J. Amer. Chem. Soc.*, 1955, **77**, 2420; Kumamoto and Westheimer, *ibid.*, p. 2515; Westheimer, *Chem. Soc. Special Publ.*, No. 8, 1957, 1.
[5] Bunton, Llewellyn, Oldham, and Vernon, *J.*, 1958, 3574.
[6] Vernon, *Chem. Soc. Special Publ.*, No. 8, 1957, 17.

Acid-catalysed Exchange.—When the pH is low we can neglect the exchange of the monoanion. Exchange is then due to reaction of the undissociated species, H_3PO_4, and its conjugate acid. The value of k_N has already been estimated. By subtracting this value from k_E we obtain ($k_E - k_N$), the first-order rate constant for the acid-catalysed exchange. The rate increases sharply with increasing hydrogen-ion concentration (Fig. 2). However, this exchange fits neither of the limiting forms of acid-catalysis predicted by the Zucker–Hammett hypothesis,[7] *i.e.*, linear dependence of rate on $[H^+]$ or upon Hammett's acidity

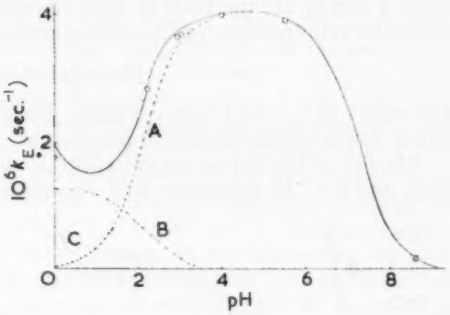


FIG. 1. *Oxygen exchange of orthophosphate at* pH 0—9 *and* 100·1°.

Contribution of (A) *exchange of monoanion,* (B) *neutral exchange, and* (C) *acid-catalysed exchange. Full line is calculated curve* (*see text*).

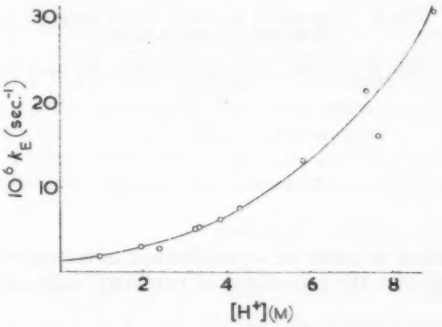


FIG. 2. *Dependence of rate of oxygen exchange of orthophosphate on acidity.*

function, h_0. A plot of log ($k_E - k_N$) against log $[H^+]$ is a straight line of slope 1·9, and against $-H_0$ it is a curve of continuously decreasing slope (Fig. 3). Since the rates with hydrochloric and perchloric acids are almost the same (Table 1), it appears that nucleophilic catalysis by anions of the strong acids is absent.

TABLE 1. *Perchloric-acid catalysed exchange at* 100·1°.

$[H^+]$ (M)	0·99	1·97	2·40	3·26 *	3·34	3·86 †	4·31	5·82	7·35	7·61	8·93
$[KH_2PO_4]$ (M)	0·38	0·37	0·76	0·40	0·37	0·74	0·38	0·38	0·37	0·38	0·37
$10^6 k_E$ (sec.$^{-1}$)	1·76	2·91	2·71	5·00	5·26	6·17	7·48	13·1	21·4	16·1	30·9
$10^6(k_E - k_N)$ (sec.$^{-1}$)	0·48	1·63	1·43	3·72	3·98	4·90	6·20	11·9	20·1	14·8	29·6

* HCl. † Two-point run.

TABLE 2. *Effect of added sodium perchlorate.*

$[H^+]$ (M)	1·05			4·00	
μ (mole l.$^{-1}$)	1·05	3·05	5·05	4·00	7·00
$10^6 k_E$ (sec.$^{-1}$)	1·78 *	1·66	2·18	6·38 *	11·0

* Interpolated values.

The acid-catalysed exchange is strongly catalysed by added sodium perchlorate (Tables 1 and 2), although this salt does not increase the rate at pH 0, where the undissociated

[7] Long and Paul, *Chem. Rev.*, 1957, **57**, 935.

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acid, H_3PO_4, is the reactive species. It seems, therefore, that the lack of proportionality between the rate and acid concentration (Figs. 2 and 3) may arise from a salt effect of the fully ionised perchloric acid since, at a constant ionic strength, $\mu = 7$, the rate is approximately proportional to the hydrogen-ion concentration. For reactions in not very dilute solutions, the dependence of rate on ionic strength has the form [8]

$$v = v_0 \exp \beta\mu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where v and v_0 are the rates at ionic strengths μ and zero respectively. Therefore, the first-order rate constant for the acid-catalysed exchange should be given by

$$(k_E - k_N) = k_A[H^+] \exp \beta\mu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The values of k_A and β were calculated from the rates of exchange in 4M-perchloric acid and in that acid plus 3M-sodium perchlorate: $10^7 k_A = 5{\cdot}45$ sec.$^{-1}$ mole^{-1} l., and $\beta = 0{\cdot}212$.

The line of Fig. 2 is a plot calculated from equation (2) by using the calculated values of k_A and β. The agreement with experiment is good, and, therefore, the kinetic form

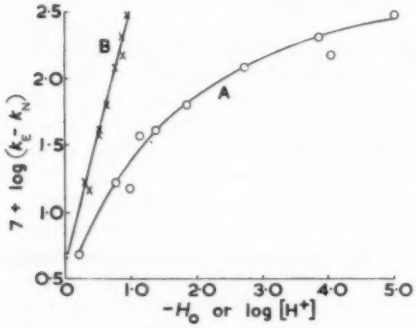

FIG. 3. *Dependence of rate of oxygen exchange on Hammett's acidity function.*

Plot of log $(k_E - k_N)$ *against* (A) $- H_0$ *and* (B) log $[H^+]$.

of the acid-catalysed exchange can be explained in terms of a positive salt effect superimposed upon the acid catalysis; this implies that the salt effects of perchloric acid and sodium perchlorate are very similar.

It has recently been suggested that explicit account should be taken of the activity of water in interpreting the catalytic effect of strong acids. For several reactions it is found [9] that plots of log $(k + H_0)$ against the activity of water have non-zero slopes, *i.e.*, $w \neq 0$. The value of w is often nearly integral and is thought to represent the differing numbers of water molecules in the initial and the transition states. A plot of log $[(k_E - k_N) + H_0]$ against log a_{H_2O} is a straight line of slope $w = 3{\cdot}9$. For the acid hydrolysis of methyl phosphate, $w = 6$. The significance of this value is, however, uncertain because this hydrolysis proceeds by two distinct reactions with different positions of bond fission.[5]

Mechanisms of Exchange.—The oxygen exchange of phosphoric acid is a reaction which is analogous to the hydrolysis of a monoalkyl phosphate proceeding with phosphorus–oxygen bond fission [4,5] (*i.e.*, the reactions involve the separation from the phosphorus atom of the groups OH and OR respectively). For reactions of the mono-negative anions, the values of k_M are $4{\cdot}03 \times 10^{-6}$ sec.$^{-1}$ and $8{\cdot}23 \times 10^{-6}$ sec.$^{-1}$ for phosphate exchange and hydrolysis of methyl phosphate, respectively.[5] Hydrogen-bonded intermediates are thought to be important in the hydrolysis of the monoanion,[4,5] and intermediates of similar structure can be postulated for the oxygen exchange of the mono-negative anion, $H_2PO_4^-$.

Although the exchange of the monoanion is very similar to the hydrolysis of the

[8] Long and McDevitt, *Chem. Rev.*, 1952, **51**, 119.
[9] Bunnett, *J. Amer. Chem. Soc.*, 1960, **82**, 499.

monoanion of methyl phosphate, there are marked differences between the mechanisms for the neutral molecules. The hydrolysis of undissociated methyl dihydrogen phosphate is almost swamped by the hydrolyses of the monoanion and the conjugate acid,[5] whereas the exchange of the undissociated orthophosphoric acid can be easily observed. The overall rate constants, k_N, are $1{\cdot}3 \times 10^{-6}$ sec.$^{-6}$ and *ca.* $0{\cdot}5 \times 10^{-6}$ sec.$^{-1}$ for oxygen exchange and hydrolysis of methyl phosphate, respectively, but these values are not strictly comparable because the ester hydrolysis is by predominant alkyl–oxygen bond fission and, moreover, is subject to a large positive salt effect.[5] Thus, oxygen exchange is much faster than hydrolysis with phosphorus–oxygen bond fission. This may be because hydrolysis requires breaking of the bond between the alkoxy-group and the phosphorus atom, whereas formation of a quinquecovalent intermediate, followed by a rapid proton-transfer, will give oxygen exchange. (We assume both processes to be bimolecular.)

The values of the rate constants for the acid-catalysed oxygen exchange of orthophosphoric acid and the corresponding values for the hydrolysis of the monomethyl ester are similar: $10^6 k_A = 5{\cdot}47$ for the exchange and 3·08 l. mole^{-1} sec.$^{-1}$ for hydrolysis.[5] However, there are differences between the two processes, because for the component of hydrolysis by phosphorus–oxygen bond fission $10^6 k_A \approx 1$ l. mole^{-1} sec.$^{-1}$. Further, whereas the oxygen exchange shows a positive salt effect, there is no salt effect upon the acid-hydrolysis of the ester. The acid-hydrolysis of methyl phosphate is accompanied by an oxygen exchange of the ester, presumably by a mechanism similar to that of the exchange of orthophosphoric acid itself. These reactions may be formulated as synchronous displacements of a water molecule by a water molecule from the solvent, or as the formation of a quinquecovalent intermediate.[5] A unimolecular decomposition of the conjugate acids seems improbable, because of the kinetic form of the acid catalysis.

Oxygen exchange does not occur to any appreciable extent by attack of one ion or molecule of a phosphate upon another (cf. ref. 1). Consistently, oxygen exchange is of the first order with respect to orthophosphate (Tables 1 and 3), and higher orders are observed only for high concentrations of orthophosphoric acid.[3]

TABLE 3. *Rate of exchange at* 100·1°, pH > 0

pH	0 *	2·21	2·96	3·1	4·00	5·51	8·61
$[KH_2PO_4]$ (M) ...	0·380	0·382	0·291	0·610	0·290	0·301	0·282
$10^6 k_E$ (sec.$^{-1}$)	1·76	2·83	3·65	3·67	4·00	3·91	0·16

The pH value is that measured at 20°. * 0·99M-$HClO_4$.

EXPERIMENTAL

The rates of oxygen exchange were measured at 100·1°, $H_2{}^{18}O$ being used. A weighed amount of potassium dihydrogen phosphate was dissolved in a known volume of $H_2{}^{18}O$, and either mineral acid or alkali added. Any precipitate of potassium perchlorate was centrifuged off. For the exchange catalysed by perchloric or hydrochloric acid, the hydrogen-ion concentration was calculated on the assumption that the phosphoric acid was undissociated. The pH values, where required, were measured with a glass electrode. Portions of the solution, in sealed tubes, were heated and potassium dihydrogen phosphate was isolated by one of three methods.

(*a*) A modification of Cohn's method,[10] in which barium phosphate is first precipitated and then converted into potassium dihydrogen phosphate.[5]

(*b*) The diluted solution was neutralised with potassium hydroxide to pH 8—10. The precipitate of potassium perchlorate was removed, and the pH of the solution adjusted to pH 5 by addition of 2M-hydrochloric acid. Impure potassium dihydrogen phosphate, contaminated with the perchlorate, was precipitated by ethanol. This precipitate was treated at 0° with insufficient water to dissolve the same weight of pure potassium dihydrogen phosphate. The undissolved perchlorate was centrifuged off and the dihydrogen phosphate precipitated by ethanol.

[10] Cohn, *J. Biol. Chem.*, 1949, **180**, 771.

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(*c*) No potassium perchlorate was present in the experiments at pH 5·51 and 8·61 and, therefore, we were able to precipitate the pure phosphate by the direct addition of ethanol.

The dried potassium dihydrogen phosphate was equilibrated isotopically with carbon dioxide [5] and this gas was analysed mass-spectrometrically; a small correction was applied for isotopic dilution by carbon dioxide.

In all our experiments the water was in large excess over the phosphate, and the first-order rate constant for oxygen exchange, irrespective of tracer, is calculated from:

$$k_E = 4 \times (2{\cdot}3/t) \log N_\infty/(N_\infty - N_t)$$

where t is the time, in seconds, and N_∞ and N_t are the isotopic abundances of the phosphate at times ∞ and t respectively, expressed in atom % excess above normal. The factor of 4 arises because k_E is four times the value of the first-order rate constant for equilibration of the tracer.

N_∞ was calculated from the isotopic abundance of the water and the relative amounts of phosphate and water. For the run with 9M-perchloric acid, its value was compared with that found experimentally: N_∞ (calc.) 0·456; N_∞ (found) 0·451 and 0·450 atom % excess, at 96 and 120 hr., respectively.

In an experiment designed to test the analytical procedure, potassium dihydrogen phosphate, prepared by reaction between phosphoric oxide and a large excess of $H_2{}^{18}O$ (0·98 atom % excess), had that isotopic abundance (mean of 5 measurements).

The experimental results for an exchange in 3·34M-perchloric acid at 100·1° were:

t (hr.)	23	46	69	92	115	138	161	∞
N (atom % excess)	0·089	0·139	0·190	0·225	0·267	0·314	0·379	0·643 (calc.)

$10^6 k_E = 5{\cdot}26$ sec.$^{-1}$ (calc. graphically).

All pH measurements were made at room temperature and, therefore, the dissociation constants of orthophosphoric acid [11] at 20° were used in calculations, *viz.*, $10^3 K_1 = 7{\cdot}90$ mole l.$^{-1}$, $10^8 K_2 = 6{\cdot}06$ mole l.$^{-1}$.

The rate constants k_M and k_N were calculated from the values of k_E at pH 2·21 and 4·00 (at 20°), and the relative amounts of H_3PO_4 and $H_2PO_4^-$ as estimated by using the above values of K_1 and K_2. Activity effects were ignored.

The full-line curve in Fig. 1 was obtained by using the following calculated molar percentages of $H_2PO_4^-$:

pH	0	1	2	3	4	5	6	7	8	9
$H_2PO_4^-$ (%)	0·78	7·32	44·1	88·8	98·7	99·3	94·3	62·3	14·2	1·62

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[*Received, August 20th,* 1960.]

[11] Nims, *J. Amer. Chem. Soc.*, 1933, **55**, 1946; 1934, **56**, 1110.

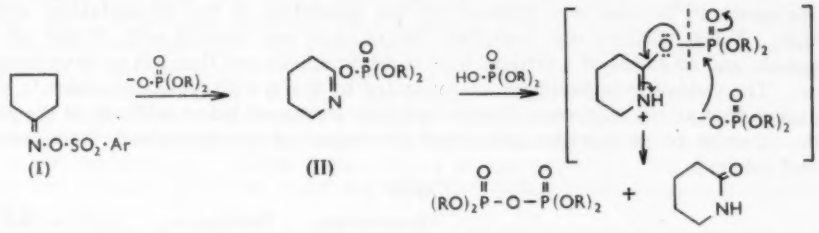
319. *Reactions between O-Benzenesulphonyl-lactims and Phosphates.*

By R. J. W. Cremlyn.

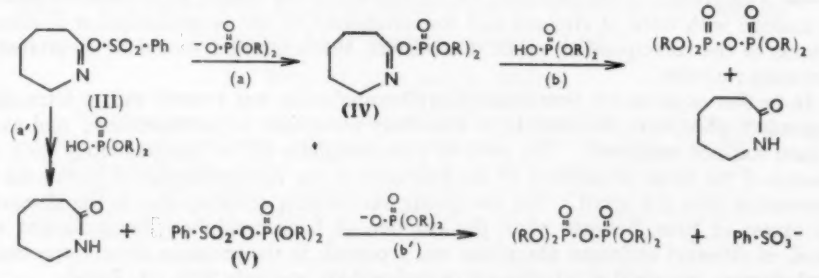
Several *O*-benzenesulphonyl-lactims have been treated with diesters of phosphoric acid and an excess of a tertiary base in nitromethane solution. The hexanolactam derivative gave the highest yields of pyrophosphates. Yields from similar reactions employing tetra-alkylammonium phosphates without an excess of base were smaller.

One method [1] for the preparation of pyrophosphates utilises spontaneous Beckmann rearrangement of a ketoxime benzenesulphonate, preferably cyclopentanone oxime *p*-nitrobenzenesulphonate [2] (I; Ar = *p*-$NO_2 \cdot C_6H_4$) in a polar solvent at room temperature. The reaction probably proceeds in stages, as shown, although the intermediate imidoyl phosphate (II) has not been isolated.

The optimum preparative conditions were found to require the use of 2 mol. of the phosphate and 1 mol. of triethylamine in anhydrous nitromethane. This procedure has also been extended to the production of unsymmetrical P^1P^2-pyrophosphates, though in



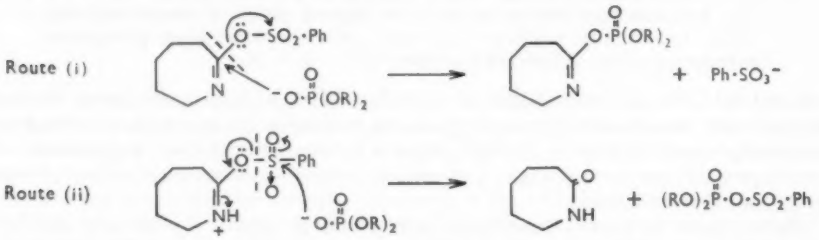
considerably lower yields.[1] A modification of this scheme has now been investigated: the lactams, prepared by Beckmann rearrangement of cyclic oximes, were converted into imidoyl benzenesulphonates (*e.g.*, III) by reaction with benzenesulphonyl chloride as described by Oxley, Peak, and Short.[3] Subsequent treatment with 2 mol. of a secondary phosphate in the presence of an excess of a tertiary base and in a polar solvent yielded pyrophosphates. Two routes for phosphorolysis of *O*-benzenesulphonylhexanolactim can be envisaged. Neither of the intermediates (IV) and (V) has been isolated, and therefore in both cases the speeds of stages a and b (or a′ and b′) are probably comparable.



The presence of an excess of a tertiary base increases the yield of pyrophosphate, so the phosphorolysis of benzenesulphonyl-lactims is base-catalysed, in contrast to the phosphorolysis of ketoxime benzenesulphonates. As the latter reaction is generally

[1] Kenner, Todd, and Webb, *J.*, 1956, 1231.
[2] Oxley and Short, *J.*, 1948, 1514.
[3] Oxley, Peak, and Short, *J.*, 1948, 1618.

regarded as proceeding by way of the imidoyl phosphate (IV) it is likely that the pyrophosphate arises from the benzenesulphonyl-lactim through the alternative route (ii) or by a combination of both routes. In either case, the function of excess of base is presumably to increase the degree of ionisation of the phosphoric acid, and consequently the ease of anion-exchange (route i; a, b) or anion attack (route ii; a′, b′):



6-Hexanolactam, valerolactam, and butyrolactam have been studied. The progress of the reaction with 1 mole of benzenesulphonyl chloride and slightly more than 1 mole of triethylamine in benzene was followed by the separation of the triethylamine hydrochloride. When reaction was complete, the mixture was treated with 2 mol. of the phosphate and an excess of a tertiary base in nitromethane and then left at room temperature. The yield of pyrophosphate was estimated by fission with cyclohexylamine.[4] Care was taken that all the sulphonyl chloride had been consumed before addition of the phosphate, in order to exclude the alternative production of pyrophosphates from arylsulphonyl halides.[5]

TABLE 1.

	Hexanolactam	Valerolactam	Butyrolactam
Lactam taken (mmoles)	4·4	5·0	4·3
* $(Ph{\cdot}CH_2{\cdot}O)_2PO_2H$ (mmoles)	8·8	10·0	8·6
Pyrophosphate yield (%)	90	80	55

* In similar experiments with $(PhO)_2PO_2H$ the pyrophosphate yields were 29, 16, and 0 respectively.

The results, summarised in the Table, show that the yield of pyrophosphate decreases sharply with decreasing ring-size of the lactam. An increasing proportion of *N*-benzenesulphonylation may be responsible; this side-reaction would be favoured as the ring-size decreases from 7 to 5 according to the concepts of Brown, Brewster, and Schechter.[6] *O* ⟶ *N*-Migration of the sulphonyl or phosphoryl group cannot be responsible because, by analogy with work of Huisgen and Reinertshofer,[7] on the isomerisation of *N*-nitrosolactams to the corresponding cyclic diazo-esters, this migration should be facilitated by increasing ring-size.

In further experiments benzenesulphonylhexanolactim was treated with a tetra-alkylammonium phosphate, followed by a secondary phosphate in nitromethane; and excess of base was not employed. The yield of pyrophosphate fell to approximately 25% and reversal of the order of addition of the reactants to the benzenesulphonyl-lactim did not appreciably alter the result. The low yields were almost certainly due to the absence of the excess of base, because when the reaction of benzenesulphonylhexanolactim with 2 mol. of dibenzyl hydrogen phosphate was repeated, in the presence of only one mol. of triethylamine, the yield of tetrabenzyl pyrophosphate was only 30% (cf. Table).

The benzenesulphonyl-lactims were brown oils incapable of purification and therefore the action of various sulphonyl chlorides on hexanolactam was studied. The relative

[4] Corby, Kenner, and Todd, *J.*, 1952, 1234.
[5] Corby, Ph.D. Thesis, Cambridge, 1952.
[6] Brown, Brewster, and Schechter, *J. Amer. Chem. Soc.*, 1954, **76**, 467.
[7] Huisgen and Reinertshofer, *Annalen*, 1952, **575**, 197.

times required for 90% completion of reaction (estimated from the precipitation of triethylamine hydrochloride) were: methanesulphonyl chloride, 5 min.; *p*-acetamidobenzenesulphonyl chloride, 20 min.; *p*-nitrobenzenesulphonyl chloride, 2½ hr.; benzenesulphonyl chloride, 12 hr.; toluene-*p*-sulphonyl chloride, 50% after 46 hr. (this reaction did not go to completion). The products were not solid, and only from the benzenesulphonyl derivatives were appreciable quantities of pyrophosphates produced under standard conditions of phosphorolysis.

Experimental

Tetrabenzyl Pyrophosphate.—Benzenesulphonyl chloride (0·58 c.c., 4·4 mmoles) was added to a solution of hexanolactam [3] (0·50 g., 4·4 mmoles) in dry benzene (2 c.c.) and triethylamine (0·80 c.c., 5·0 mmoles) with external cooling. After 12 hr. at room temperature filtration yielded triethylamine hydrochloride (0·520 g., 93%). The brown liquor was diluted with nitromethane (6 c.c.), treated with dibenzyl hydrogen phosphate (2·4 g., 8·8 mmoles) and triethylamine (1·9 c.c., 3 mmoles), and left for 19 hr. at room temperature, then extracted with chloroform (200 c.c.). The extract was washed with 50% aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated *in vacuo*. Treatment with cyclohexylamine (2 c.c.) in benzene (8 c.c.) gave, after 12 hr., crystalline cyclohexylammonium dibenzyl phosphate (1·36 g., 90%). The filtrate therefrom, when worked up as usual,[4] gave a brown oil (0·213 g.).

Tetraphenyl Pyrophosphate.—Anhydrous tetraethylammonium diphenyl phosphate (0·880 g., 2·2 mmoles) in nitromethane (4 c.c.) was added to a benzene solution of *O*-benzenesulphonylhexanolactim (prepared from 0·250 g. of the lactam). After 2 days at room temperature, anhydrous diphenyl hydrogen phosphate (0·550 g., 2·2 mmoles) was added, and the mixture left for a further 3 days at room temperature. After the usual working-up, the neutral fraction was treated overnight with cyclohexylamine (1 c.c.) in benzene (4 c.c.); this gave cyclohexylammonium diphenyl phosphate (0·430 g., 56%) and diphenyl cyclohexylphosphoramidate (0·134 g., 19%).

These examples illustrate the general procedure for the experiments summarised in the Table.

My thanks are offered to the University of Wales for a University Fellowship and to Professor Sir Alexander Todd, F.R.S., and Professor G. W. Kenner for their interest.

Brunel College of Technology, London, W.3. [*Received, September 26th*, 1960.]

[3] Eck and Marvel, *Org. Synth.*, Coll. Vol. II, 1st edn. 1943, p. 371.

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320. 3-*Acetamido*-3-*deoxy*-D-*allose Diethyl Dithioacetal and its Oxidation by Peroxypropionic Acid.*[1]

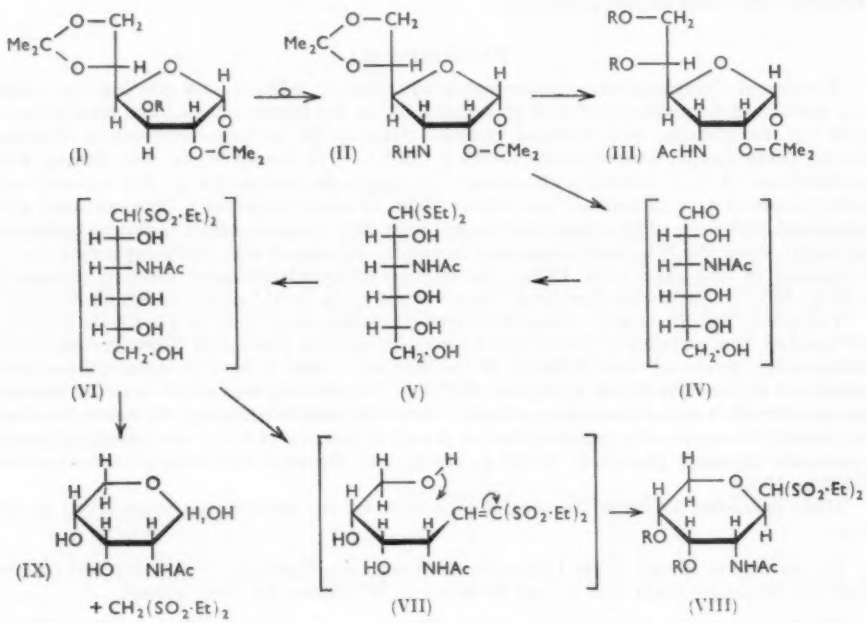
By Bruce Coxon and L. Hough.

The reactions of 1,2:5,6-di-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranose with ammonia and with hydrazine proceed with inversion at $C_{(3)}$ to give D-allofuranose derivatives. The products were converted into 3-acetamido-3-deoxy-D-allose diethyl dithioacetal which was oxidised with peroxypropionic acid to a mixture of (2-acetamido-2-deoxy-β-D-ribopyranosyl)-diethylsulphonyl methane, 2-acetamido-2-deoxy-D-ribose, and diethylsulphonylmethane. The mechanism of this reaction is discussed.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranose (I; R = tosyl) reacts with ammonia,[2] dimethylamine,[3] and hydrazine [4] by nucleophilic substitution of the toluene-*p*-sulphonyloxy-group to give the 3-amino-, 3-dimethylamino-, and 3-hydrazino-derivatives,

[1] For a preliminary account of some of this work, see Coxon and Hough, *Chem. and Ind.*, 1959, 1249.
[2] Freundenberg, Burkhart, and Braun, *Ber.*, 1926, **59**, 714.
[3] Freundenberg and Smeykal, *Ber.*, 1926, **59**, 100.
[4] Freundenberg and Brauns, *Ber.*, 1922, **55**, 3233.

in which Freundenberg *et al.* considered that the D-*gluco*-configuration was retained. This view persisted [5,6] until 1956, when Cope and Shen [7] questioned the assumed stereochemical course of the reaction on the basis of a study of the differences in reactivity of 1,4:3,6-dianhydrohexitol ditoluene-*p*-sulphonates with a variety of nucleophilic reagents. They found good evidence for the assignment of the S_N2 mechanism to these reactions, and



hence the reaction of the 3-*O*-tosylglucofuranose derivative (I; R = tosyl) with nucleophilic reagents was more likely to lead to stereochemical inversion at $C_{(3)}$, to give, *e.g.*, derivatives of type (II). In order to determine the stereochemical course of this reaction we have compared the diethylsulphonyl derivative prepared from the above 3-amino-3-deoxy-D-hexose with a similar derivative [8] of 3-acetamido-3-deoxy-D-altrose. The diethyl dithioacetal of the latter was oxidized with peroxypropionic acid to give, by cyclization of the intermediary D-*ribo*-3-acetamido-1,1-diethylsulphonyl-4,5,6-trihydroxyhex-1-ene (VII), (2-acetamido-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane (VIII; R = H),* which should also be obtained from the configurationally related 3-acetamido-3-deoxy-D-allose.

As in the previous work,[2] the reaction of 1,2:5,6-di-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranose (I; R = tosyl) with methanolic ammonia under pressure at 170° gave a rather impure 3-aminohexofuranose derivative in low yield (11—16%). In an effort to improve the yield of this replacement product, the reaction of 1,2:5,6-di-*O*-isopropylidene-3-*O*-(nitrobenzene-*p*-sulphonyl)-α-D-glucofuranose (I; R = nitrobenzene-*p*-sulphonyl) with

* According to a previous system of nomenclature,[9] this cyclic disulphone (VIII; R = H) would be termed D-*allo*-3-acetamido-2,6-epoxy-1,1-diethylsulphonyl 4,5-dihydroxyhexane.

[5] Peat and Wiggins, *J.*, 1938, 1810.
[6] Wolfrom, Shafizadeh, and Armstrong *J. Amer. Chem. Soc.*, 1958, **80**, 4885.
[7] Cope and Shen, *J. Amer. Chem. Soc.*, 1956, **78**, 3177.
[8] Coxon and Hough, *J.*, 1961, 1463.
[9] Hough and Taylor, *J.*, 1956, 970.

ammonia under pressure was attempted (cf. Tipson [10]), since it was expected that the *p*-nitro-substituent would facilitate electron-recession in the departing group. The only crystalline product obtained was 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, presumably formed by fission of the sulphur–oxygen bond of the sulphonyl ester, by nucleophilic attack by ammonia, at sulphur instead of at carbon,[11] resulting in retention of configuration.

Improved yields [6,12] have been obtained by treatment of 1,2:5,6-di-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranose with hydrazine at 140°, and subsequent catalytic hydrogenation of the 3-deoxy-3-hydrazino-derivative.

A more convenient reaction was obtained by boiling the 3-*O*-tosyl derivative with hydrazine under reflux in an atmosphere of nitrogen, conditions somewhat less drastic than those used previously.[4,6] The 3-deoxy-3-hydrazino-derivative was unstable in air, and so it was hydrogenated immediately to give the 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene derivative (57% yield) which was identical with that prepared by direct ammonolysis. The 3-amino-3-deoxy-derivative with acetic anhydride–pyridine gave the 3-acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-hexose.†

Treatment of this 3-acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidenehexose with ethanethiol and hydrochloric acid at 0° for 24 hr. afforded the 3-acetamido-3-deoxyhexose diethyl dithioacetal. Oxidation of the latter by peroxypropionic acid in methanol at either −20° or −10° gave a mixture of (2-acetamido-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane (VIII; R = H), 2-acetamido-2-deoxy-D-ribose (IX), and diethylsulphonylmethane, which was separated by either paper chromatography or solvent extraction. The cyclic disulphone (VIII; R = H), its di-*O*-acetate (VIII; R = Ac), and 2-acetamido-2-deoxy-D-ribose were identical with those prepared previously [8] from 3-acetamido-3-deoxy-D-altrose diethyl dithioacetal.

Thus application of a series of reactions to the diethyl dithioacetals of 3-acetamido-3-deoxy-D-altrose [8] and 3-acetamido-3-deoxy-D-allose, involving modifications of the asymmetry only at position 2, established without doubt that the ammonolysis and hydrazinolysis of 1,2:5,6-di-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranose (I; R = tosyl) proceeded with stereochemical inversion at position 3 to give derivatives of α-D-allofuranose (II).

An alternative proof of this inversion was described by Lemieux and Chu [12] who converted the 3-deoxy-3-hydrazino-derivative (II; R = NH_2) through the 3-amino-3-deoxy-derivative (II; R = H) into 3-amino-3-deoxy-D-ribose.

In order to establish firmly that the di-*O*-acetate (VIII; R = Ac) was not a derivative of the hex-1-ene (VII), the acetate (XII) of the latter was prepared by a method used by MacDonald and Fischer [13] to prepare D-*arabo*-3,4,5,6-tetra-*O*-acetyl-1,1-diethylsulphonylhex-1-ene.

Acetylation of 3-acetamido-3-deoxy-D-allose diethyl dithioacetal (V) in pyridine–acetic anhydride afforded 3-acetamido-2,4,5,6-tetra-*O*-acetyl-3-deoxy-D-allose diethyl dithioacetal (X) which, on oxidation with peroxypropionic acid, yielded D-*ribo*-3-acetamido-4,5,6-tri-*O*-acetyl-1,1-diethylsulphonylhex-1-ene (XII) through the intermediary saturated 1,1-diethylsulphonyl derivative (XI) which had lost the elements of acetic acid. This hex-1-ene derivative (XII) differed from the di-*O*-acetate of the cyclic disulphone (VIII; R = Ac).

The formation of 2-acetamido-2-deoxy-D-ribose in the oxidations of 3-acetamido-3-deoxy-D-altrose [8] and 3-acetamido-3-deoxy-D-allose diethyl dithioacetal was a novel feature of these reactions, since it occurred under non-alkaline conditions. This pentose derivative probably arose from the acyclic saturated disulphones (*e.g.*, VI) since these are

† When a solution of this product in chloroform was washed with dilute acid, 3-acetamido-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (III; R = H) was obtained as a by-product, and was characterized as 3-acetamido-5,6-di-*O*-acetyl-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (III; R = Ac).

[10] Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 211.
[11] Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1956, p. 281.
[12] Lemieux and Chu, *J. Amer. Chem. Soc.*, 1958, **80**, 4745.
[13] MacDonald and Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 2087.

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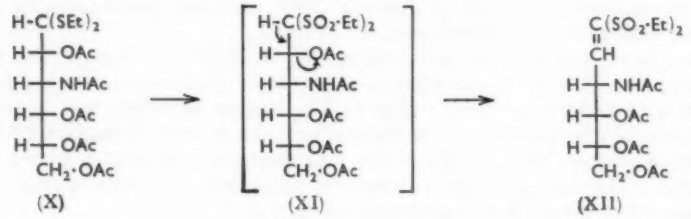
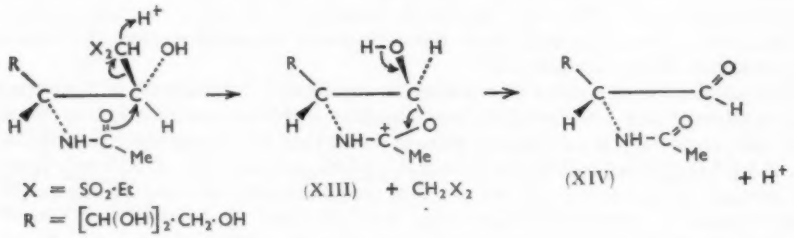
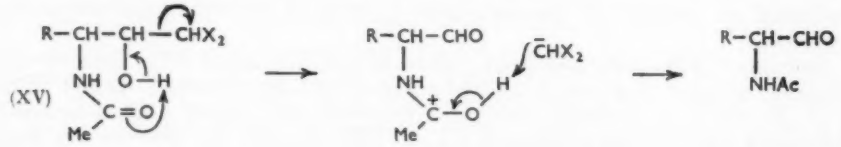
the most sensitive of the disulphones to cleavage with concomitant formation of diethylsulphonylmethane.[9] Since oxidations of D-altrose diethyl dithioacetal under the same conditions[14] did not produce any cleavage to pentose, it appears that the acetamido-group facilitated the production of 2-acetamido-2-deoxy-D-ribose by a reaction which was competitive with the formation of the 1,1-diethylsulphonylhex-1-ene (VII).



Neighbouring-group participation is possible in which the amide-oxygen attacks $C_{(2)}$ (which will be cationoid because of adjacent electrophilic substituents) with simultaneous ejection of the diethylsulphonylmethyl anion to give a cyclic carbonium ion (XIII) which would then collapse to give 2-acetamido-2-deoxy-D-ribose (XIV).



Alternatively, the weakly basic properties of the amide group could assist in the removal of the hydrogen of the hydroxyl at $C_{(2)}$ of the saturated disulphone (XV).



Pauling[15] has assessed the basic constant of amides as approximately 1×10^{-20} and this very weak basicity is almost certainly due to protonation of the carbonyl-oxygen atom, since addition of a proton to the nitrogen atom would inhibit the resonance of the amide group.[16]

Experimental

Details relevant to chromatography, presentation of infrared data, etc., are given in the preceding paper.[9]

1,2:5,6-*Di*-O-*isopropylidene*-3-O-*nitrobenzene*-p-*sulphonyl*-α-D-*glucofuranose* (I; R = nitrobenzene-*p*-sulphonyl).—1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (21·3 g.) in dry pyridine

[14] Coxon and Hough, unpublished results.
[15] Pauling, "The Nature of the Chemical Bond," Oxford University Press, London, 1940, 208.
[16] Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, 1955, 361.

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(20 ml.) was cooled to 0° and a solution of nitrobenzene-*p*-sulphonyl chloride (20 g.; 1·1 mol.) in dry pyridine (25 ml.) was added dropwise with cooling and stirring. At this stage, the mixture was diluted with chloroform (10 ml.) to decrease its viscosity and kept at room temperature with stirring for 26 hr. Water was then added in small quantities with cooling and stirring, and the solution was poured into water and extracted with chloroform (4 × 100 ml.). The combined extracts were washed successively with cooled 2N-hydrochloric acid (2 × 200 ml.), saturated sodium hydrogen carbonate solution, and water, and dried (Na_2SO_4). Concentration gave a brown syrup which, after decolorization, crystallized as square prisms (29·8 g., 82%), m. p. 106—109°. Recrystallized twice from aqueous ethanol, the *sulphonate* had m. p. 110°, $[\alpha]_D$ −81·2° (*c* 3·99) (Found: C, 48·8; H, 5·1; N, 2·9. $C_{18}H_{23}NO_{10}S$ requires C, 48·5; H, 5·2; N, 3·1%).

Attempted Ammonolysis of the Nitrobenzene-p-*sulphonate.*—The sulphonate (12 g.) was suspended in methanol (500 ml.) saturated with anhydrous ammonia at *ca.* −30° (acetone–carbon dioxide). The mixture was sealed in a steel autoclave and heated at 165°/40 atm. for 45 hr. The dark brown solution was then concentrated to a black tar, to which 15% w/v potassium hydroxide (90 ml.) was added, and the mixture was extracted with ether (4 × 100 ml.). Concentration of the combined ethereal extracts gave a brown syrup which was decolorized and crystallized, giving needles of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1·2 g., 17%), m. p. 107—109°, depressed to 94° on admixture with starting material. Washed with ether, the crystals had m. p. 110—111°, undepressed on admixture with authentic di-*O*-isopropylidene-α-D-glucofuranose.

*3-Deoxy-3-hydrazino-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose* (II; R = NH_2).—1,2:5,6-Di-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranose (20 g.) was heated under reflux for 25 hr. with 98% hydrazine (50 ml.) in a stream of oxygen-free nitrogen. The clear solution was then allowed to cool and extracted with ether (3 × 50 ml.), and the combined extracts were washed with 50% w/v potassium hydroxide (10 ml.) and dried (K_2CO_3). Concentration followed by drying at room temperature/1 mm. gave white crystals (11·0 g., 83%) which, after being washed with a little cold ether, had m. p. 97—100°, R_F 0·96 (solvent iii; sprays *a* and *c*). The hydrazino-derivative reduced Tollens's reagent in the cold and Benedict's reagent when heated, but was unstable in air; consequently each product was immediately reduced to the 3-amino-derivative.

*3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose* (II; R = H).—The hydrazino-derivative (11 g.) in ethanol (200 ml.) was hydrogenated in the presence of Raney nickel catalyst (15 g.), at 65 lb. per sq. in. for 18 hr. at *ca.* 80° in the Edwards apparatus. The catalyst was then filtered off through Celite filter aid, and the ethanolic solution concentrated to a crystalline residue, which, recrystallized from ethanol–light petroleum (b. p. 40—60°), yielded the 3-amino-derivative as needles (7·15 g., 69%). A further recrystallization from the same solvent pair gave the pure product which had m. p. 92—93°, $[\alpha]_D$ +32·7° (*c* 2·39), R_F 0·84 (solvent iii; spray *a*) (Found: C, 55·4; H, 8·0; N, 5·1. Calc. for $C_{12}H_{21}NO_5$: C, 55·6; H, 8·2; N, 5·4%). This amino-derivative was also prepared in 11% yield by the reaction [8] of methanolic ammonia with 1,2:5,6-di-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranose at 170° and had m. p. and mixed m. p. 91—93°, $[\alpha]_D$ +36° (*c* 1·25).

*3-Acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose* (II; R = Ac).—To a solution of 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (2·53 g.) in dry pyridine (15 ml.) was added acetic anhydride (15 ml.), and the mixture kept at room temperature for 13 hr., then poured into ice-water and extracted into chloroform (4 × 30 ml.). The combined extracts were washed successively with cold 2N-hydrochloric acid (3 × 30 ml.), saturated sodium hydrogen carbonate (30 ml.), and water, and then dried (Na_2SO_4). The pale yellow syrup obtained on concentration crystallized immediately, and was decolorized. Recrystallization from light petroleum (b. p. 80—100°) containing a little ethanol gave the *N*-acetyl derivative as rods (2·15 g., 73%), m. p. 130°, $[\alpha]_D$ +71·8° (*c* 2·12) (Found: C, 55·5; H, 7·5; N, 4·4. Calc. for $C_{14}H_{23}NO_6$: C, 55·8; H, 7·7; N, 4·6%), $\nu_{max.}$ 3370m and 1538s (NH), 1680s cm.$^{-1}$ (N-Ac). Lemieux and Chu [12] record m. p. 127—128°, and $[\alpha]_D$ +71·3°. In one particular preparation, the acetamido-derivative was impure and acetylation of this product as above, followed by crystallization from water, yielded *3-acetamido-5,6-di-*O*-acetyl-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose* (III; R = Ac) as needles, m. p. 162—164°. Recrystallized from water, the triacetate had m. p. 164—165°, depressed to 120—140° on admixture with the di-*O*-isopropylidene derivative, and had $[\alpha]_D$ +63·9° (*c* 2·00) (Found: C, 51·9; H, 6·7; N, 4·3. $C_{18}H_{29}NO_9$ requires C, 52·2; H, 6·7; N, 4·1%), $\nu_{max.}$ 3400m and 1530s (NH), 1753s and 1730s (*O*-Ac), 1680s cm.$^{-1}$

N-Ac). Later experience suggested that a better procedure for isolating the *N*-acetate of the di-*O*-isopropylidene-amino-derivative was to omit the acid-washing of the chloroform extract.

3-Acetamido-3-deoxy-1,2-O-isopropylidene-α-D-allofuranose (III; R = H).—The triacetate (1·22 g.) was dissolved in methanol (40 ml.) and aqueous ammonia (40 ml.; *d* 0·88) was added. The mixture was kept at room temperature for 38 hr.; ammonia was then removed under reduced pressure, and acetate ions by passage of the solution through Amberlite IR-4B(OH) resin. Concentration gave a brown syrup which crystallized after decolorization as needles (0·68 g., 74%). Recrystallized twice from methanol–ether, the *N*-acetyl derivative had m. p. 158—159°, $[\alpha]_D$ +150° (*c* 1·89 in H_2O), R_{Rh} 1·7 (solvent i; spray *b*) (Found: C, 50·4; H, 7·3; N, 5·4; Ac, 18·5. Calc. for $C_{11}H_{19}NO_6$: C, 50·5; H, 7·3; N, 5·4; Ac, 16·5%). Lemieux and Chu [12] record m. p. 157—158°.

Periodate oxidation gave the following results:

Time (hr.)	0·5	18·5	43
IO_4 consumed (mole)	0·92	1·01	1·01

3-Acetamido-3-deoxy-D-allose Diethyl Dithioacetal (V).—3-Acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (1·5 g.) was treated with ethanethiol (8 ml.) and cooled to 0°. Concentrated hydrochloric acid (10 ml.; *d* 1·18) was added and the mixture shaken at 0°. After 24 hr., the mixture was diluted with methanol (100 ml.) and neutralized (lead carbonate), and the insoluble residues were filtered off and washed with hot methanol (150 ml.). Concentration of the combined filtrate and washings gave a white solid which was recrystallized from ethanol–light petroleum (b. p. 80—100°) and washed with a little light petroleum, yielding the *dithioacetal* as plates (0·9 g., 55%); recrystallized from ethanol–light petroleum (b. p. 80—100°), this had m. p. 160°, $[\alpha]_D$ −24·5° (*c* 1·88 in MeOH), R_{Rh} 1·9 (solvent i; sprays *b* and *c*) (Found: C, 44·1; H, 7·9; N, 4·0; S, 19·6; Ac, 15·4, 15·4. $C_{12}H_{25}NO_5S_2$ requires C, 44·0; H, 7·7; N, 4·3; S, 19·6; Ac, 13·2%).

Oxidation of 3-Acetamido-3-deoxy-D-allose Diethyl Dithioacetal by Peroxypropionic Acid.—The dithioacetal (0·74 g.) in methanol (20 ml.) was cooled to −20° (ice–salt), aqueous peroxypropionic acid (12 ml.) added dropwise with shaking, and the mixture kept at −20° for 1 hr. Concentration gave a hygroscopic syrup from which traces of peroxypropionic acid were removed by repeated dissolution in methanol and reconcentration (yield 0·94 g.). Paper chromatography of the syrup with spray *b* showed the presence of two components, R_{Rh} 1·1 and 1·5 (solvent iv) and R_P 0·44 and 0·63 (solvent i). Two methods of working up were used.

(a) *By paper chromatography.* The syrup (0·75 g.) was separated by chromatography on three large sheets of Whatman 3MM filter paper, solvent i being used for 22 hr. and the acetamido-derivatives were extracted from the appropriate parts of the chromatograms with hot methanol. The slower-moving component (R_P 0·44) was obtained as a syrup (0·119 g.) which slowly crystallized, yielding fine needles (0·064 g.) of 2-acetamido-2-deoxy-D-ribose. Recrystallized thrice from methanol–ether, the pentose derivative had m. p. 138—141°, $[\alpha]_D^{26}$ −69° (2 min.) ⟶ −36° (15 min. final, *c* 0·90 in H_2O), R_P 0·44 [solvent i; sprays *b*, *d* (orange spot), and *e* (violet spot)] (Found: C, 44·2; H, 7·0; N, 7·3; Ac, 20·6. Calc. for $C_7H_{13}NO_5$: C, 44·0; H, 6·9; N, 7·3; Ac, 22·5%), $\nu_{max.}$ 3440s and 3350s (OH and NH), 1565s (NH), 1600s cm.$^{-1}$ (*N*-Ac). It had identical infrared spectrum and mixed m. p. 136—139° with the product (m. p. 136—139°) obtained by oxidation of 3-acetamido-3-deoxy-D-altrose diethyl dithioacetal.[8] Kuhn and Baschang [17] record m. p. 141—143°, $[\alpha]_D$ −73·2° (2 min.) ⟶ −39° (1 hr.).

The faster-moving component (R_P 0·63) was a syrup (0·344 g.) which partially crystallized on trituration with methanol, giving needles, m. p. 101—102° undepressed on admixture with authentic diethylsulphonylmethane. The mother-liquors were diluted with water (50 ml.) and extracted with benzene (3 × 20 ml.). Concentration of the benzene extracts gave more diethylsulphonylmethane and evaporation of the aqueous layer gave a hygroscopic syrup of (2-acetamido-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane (0·27 g.), $[\alpha]_D$ −29·6° (*c* 4·60 in MeOH) (Found: C, 38·5; H, 6·1; N, 3·8; S, 17·9; Ac, 12·2%; equiv., 389. Calc. for $C_{13}H_{23}NO_8S_2$: C, 38·6; H, 6·2; N, 3·8; S, 17·2; Ac, 11·5%; *M*, 374), $\nu_{max.}$ 3520—3400s (OH and NH), 1667s (*N*-Ac), 1532 cm.$^{-1}$ (NH). The disulphone gave only a pale yellow colour with dry pyridine even after prolonged standing.

(b) *By solvent extraction.* The mixture of disulphone, pentose, and diethylsulphonylmethane was separated on a larger scale by the following procedure. (i) Cold chloroform-extraction of a

[17] Kuhn and Baschang, *Annalen*, 1959, **628**, 193.

20% aqueous solution of the syrupy mixture removed diethylsulphonylmethane and a small quantity of disulphone. (ii) Continuous chloroform-extraction of the aqueous layer for 2 days yielded pure disulphone on concentration of the extract. (iii) Evaporation of the remaining aqueous layer gave 2-acetamido-2-deoxy-D-ribose.

(*2-Acetamido-3,4-di-O-acetyl-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane* (VIII; R = Ac).—A solution of (2-acetamido-2-deoxy-β-D-ribopyranosyl)diethylsulphonylmethane (0·18 g.) in acetic anhydride (6 ml.) was heated with concentrated sulphuric acid (2 drops) at 95—100° for 0·5 hr. After cooling to room temperature, the mixture was poured into ice and sodium hydrogen carbonate and extracted with chloroform (5 × 30 ml.). The combined extracts were washed with water and dried ($CaSO_4$). Concentration gave a pale yellow syrup which was decolorized, yielding a syrup (0·2 g., 91%) which crystallized from acetone–light petroleum (b. p. 80—100°). Recrystallized from the same solvent pair and washed with ethereal acetone, the triacetate had m. p. 183—185°, $[\alpha]_D$ −17·5° (*c* 1·09) (Found: C, 41·8; H, 5·9; N, 3·0; S, 12·3; Ac, 27·6. Calc. for $C_{16}H_{27}NO_{10}S_2$: C, 42·0; H, 6·0; N, 3·1; S, 14·0; Ac, 28·2%), $\nu_{max.}$ 3300m and 1550s (NH), 1750s (*O*-Ac), 1650s cm.$^{-1}$ (*N*-Ac). The product had mixed m. p. 183—185° and was identical in infrared spectrum and *X*-ray powder photograph with the authentic specimen {m. p. 183—185°, $[\alpha]_D$ −16·8° (*c* 1·34)} obtained from 3-acetamido-3-deoxy-D-altrose.[8]

Acetylation of the syrupy disulphone (VIII; R = H) in acetic anhydride–pyridine for 3 days gave the same crystalline triacetate as described above.

3-Acetamido-2,4,5,6-tetra-O-acetyl-3-deoxy-D-allose Diethyl Dithioacetal (X).—3-Acetamido-3-deoxy-D-allose diethyl dithioacetal (1·0 g.) was suspended in dry pyridine (20 ml.) and acetic anhydride (20 ml.) added. After 19 hr. at room temperature, the mixture was poured into ice-water containing sodium hydrogen carbonate and extracted into chloroform (5 × 20 ml.). The combined extracts were washed successively with cold 2N-hydrochloric acid (2 × 50 ml.), saturated sodium hydrogen carbonate solution, and water. Concentration gave a pale yellow syrup which was decolorized. Dilution of the methanolic solution with water yielded clusters of highly reflecting needles, m. p. 124—125° (1·02 g., 67%). Recrystallized from aqueous methanol, the *penta-acetate* had m. p. 125°, $[\alpha]_D$ +30·0° (*c* 2·33) (Found: C, 48·1; H, 6·9; N, 2·8; S, 12·4; Ac, 36·8. $C_{20}H_{33}NO_9S_2$ requires C, 48·4; H, 6·7; N, 2·8; S, 12·9; Ac, 43·4%).

D-ribo-*3-Acetamido-4,5,6-tri-O-acetyl-1,1-diethylsulphonylhex-1-ene* (XII).—3-Acetamido-2,4,5,6-tetra-*O*-acetyl-3-deoxy-D-allose diethyl dithioacetal (0·56 g.) in methanol (20 ml.) was cooled to −8°, and aqueous peroxypropionic acid (6 ml.) was added. The mixture was kept at −5° for 1 hr., then concentrated to a syrup (0·61 g.) which crystallized from methanol–ether as needles, m. p. 135—137° (0·35 g., 61%). Recrystallized from methanol–ether, the *hexene* had m. p. 137°, $[\alpha]_D$ +49° (*c* 1·44) (Found: C, 43·1; H, 6·0; N, 2·8; S, 12·1; Ac, 32·9. $C_{18}H_{29}NO_{11}S_2$ requires C, 43·2; H, 5·9; N, 2·8; S, 12·9; Ac, 34·5%), $\nu_{max.}$ 3370m and 1520m (NH), 1750s (*O*-Ac), 1670s (*N*-Ac), 1620w cm.$^{-1}$ (C=C). The compound absorbed below 220 mμ.

We thank Dr. T. Bevan for the *X*-ray powder photographs, and the Ministry of Supply, Waltham Abbey, for a sample of anhydrous hydrazine, and one of us (B. C.) thanks the D.S.I.R. for a maintenance grant.

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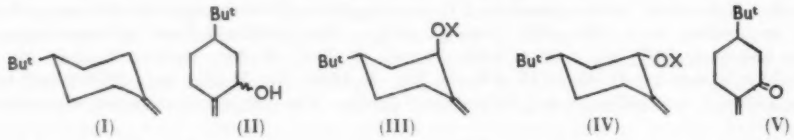
321. *Conformationally Fixed Olefins. Part III.*[1] *The Stereochemistry of the Reaction of t-Butyl Perbenzoate with 1-Methylene-4-t-butylcyclohexane.*

By B. Cross and G. H. Whitham.

The main product from the reaction of 1-methylene-4-t-butylcyclohexane (I) with t-butyl perbenzoate in the presence of cuprous chloride is the benzoate of 2-methylene-*trans*-5-t-butylcyclohexanol (III; X = H). The corresponding *cis*-alcohol (IV; X = H) is obtained by reduction of 2-hydroxymethylene-5-t-butylcyclohexanone (VI) with lithium aluminium hydride. Evidence on which the configurational assignments are made is presented and the stereochemical course of the reaction of t-butyl perbenzoate is discussed.

The reaction of an olefin, possessing an allylic hydrogen, with t-butyl perbenzoate in benzene in the presence of catalytic quantities of cuprous salts usually results in the introduction of an allylic benzoyloxy-group:[2] C:C·CH ⟶ C:C·C(OBz). Allylically rearranged products are not obtained in this reaction and a modified free-radical mechanism has been proposed.[3] So far no studies on the sterochemistry of the reaction have been reported and we have, therefore, investigated this using 1-methylene-4-t-butylcyclohexane[4] (I) as substrate. This compound, which should exist in the chair form shown,[4] is free from strong steric influences at $C_{(2)}$ so that the mode of allylic substitution should be dictated largely by stereoelectronic effects.

The crude product from the reaction of t-butyl perbenzoate with the hydrocarbon (I), which consisted of a mixture of biphenyl, unchanged hydrocarbon, and benzoates, was hydrolysed and chromatographed. The main product, obtained in 26% yield, had $\nu_{max.}$ 3580 (OH) and 3060, 1650, and 904 cm.$^{-1}$ (C=CH_2) and the conclusion that it was one of the epimeric 2-methylene-5-t-butylcyclohexanols (II) was borne out by reactions described below. A small amount of another alcohol possessing methylenic infrared absorption was also formed; this could not be obtained free from the major product but was shown to be



(I) (II) (III) (IV) (V)

the epimer of the latter by infrared comparison with a pure sample obtained later in another way. Other hydroxylic materials were also formed but were not investigated after infrared spectra had shown the absence of the exocyclic methylene group.

We made the tentative assignment, on the basis of their order of elution on chromatography,[5] that the major allylic alcohol, eluted first, was the axial isomer (III; X = H), the minor component being the equatorial epimer (IV; X = H). The possibility that epimerisation might have occurred under the alkaline conditions of hydrolysis was excluded by an alternative procedure in which lithium aluminium hydride was used.

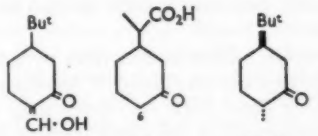
To confirm the assignments (which for convenience of discussion will be assumed to be correct), an alternative route to the minor isomer was required. Attempts to epimerise the alcohol (III; X = H) by potassium t-butoxide in t-butyl alcohol and benzophenone[6]

[1] Part II, Cross and Whitham, *J.*, 1960, 3895.
[2] Kharasch and Sosnovsky, *J. Amer. Chem. Soc.*, 1958, **80**, 756; Kharasch, Sosnovsky, and Yang, *ibid.*, 1959, **81**, 5819.
[3] Denney, Denney, and Feig, *Tetrahedron Letters*, 1959, **15**, 19.
[4] Cross and Whitham, *J.*, 1960, 3892.
[5] Barton, *J.*, 1953, 1027.
[6] Doering and Aschner, *J. Amer. Chem. Soc.*, 1949, **71**, 839.

or aluminium isopropoxide in propan-2-ol and acetone [7] resulted only in the recovery of unchanged material, and attempts to oxidise it to the methylene ketone (V) gave intractable mixtures owing to the ready dimerisation of α-methylenecyclohexanones.[8]

Dreiding and Hartman [9] have shown that 2-methylenecyclohexanol is obtained, along with 1-hydroxymethylcyclohexene and 2-hydroxymethylcyclohexanol, by reduction of 2-hydroxymethylenecyclohexanone with lithium aluminium hydride. It is likely that the 2-methylenecyclohexanol is derived by reduction of 2-methylenecylohexanone formed *in situ*. Thus a new approach to the equatorial allylic alcohol (IV; X = H) would involve reduction of 2-hydroxymethylene-5-t-butylcyclohexanone (VI) by lithium aluminium hydride, which should proceed by way of the unsaturated ketone (V).

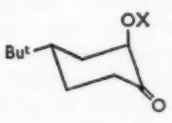
Condensation of 3-t-butylcyclohexanone [10] with ethyl formate gave the hydroxymethylene-ketone (VI). That formylation would be expected to occur as shown, and not at $C_{(2)}$, owing to the steric effect of the t-butyl group, is indicated by the analogous case [11] of the ketone (VII) where condensation occurs at $C_{(6)}$. Reduction of the hydroxymethylene-ketone (VI) with an excess of lithium aluminium hydride gave the required allylic alcohol (IV; X = H) in 33% yield. It was chromatographically homogeneous and its infrared spectrum, though different from that of the major allylic alcohol (III; X = H) obtained in the t-butyl perbenzoate reaction, was identical with that of the minor isomer. This confirmed the identity of the latter.



(VI)

(VII)

(VIII)



(IX)

(X)

It was next necessary to prove, first, that the two allylic alcohols obtained above were indeed the epimeric 2-methylene-5-t-butylcyclohexanols and, secondly, that the configurations are as tentatively assigned. Their skeletal identity was proved by their rearrangement, when heated with palladium–carbon in methanol, to the same methyl ketone (VIII). Additional confirmation that the two alcohols have the same skeleton and substantiation of the assigned configurations came from the products of ozonolysis of their 3,5-dinitrobenzoates: ozonolysis, by the procedure of Conia and Leriverend,[12] of the 3,5-dinitrobenzoate of the minor alcohol gave a crystalline ketone 3,5-dinitrobenzoate; that of the main alcohol gave a gum which had a different infrared spectrum (in particular, the gum had only one band in the carbonyl region at 1743 cm.$^{-1}$ whereas the crystalline isomer had two bands, at 1751 and 1739 cm.$^{-1}$). Treatment of the gum with 0·1N-perchloric acid in acetone gave the crystalline isomer. These results are best accommodated by an acid-catalysed epimerisation of the axial ester (IX) to the more stable equatorial 3,5-dinitrobenzoate (X).

Additional confirmation of the configurational assignments and conversely, taken in conjuction with the above chemical evidence, that the allylic alcohols (III and IV; X = H) exist predominantly in the chair form in carbon tetrachloride solution is given by their nuclear magnetic resonance spectra. For the alcohol (IV; X = H) the absorption due to the tertiary proton >CH·OH was a broad band at −122·7 cycles/sec. whereas for the alcohol (III; X = H) it was sharper and centred at −133·8 cycles/sec. Examples [13]

[7] Eliel and Ro, *J. Amer. Chem. Soc.*, 1957, **79**, 5992.
[8] Mannich, *Ber.*, 1945, **74**, 554.
[9] Dreiding and Hartman, *J. Amer. Chem. Soc.*, 1956, **78**, 1216.
[10] Whitmore and Pedlow, *J. Amer. Chem. Soc.*, 1941, **63**, 759.
[11] Abe, Harukawa, Ishikawa, Miki, Sumi, and Tuga, *J. Amer. Chem. Soc.*, 1953, **75**, 2567.
[12] Conia and Leriverend, *Compt. rend.*, 1960, **250**, 1078.
[13] Lemieux, Kullnig, Bernstein, and Schneider, *J. Amer. Chem. Soc.*, 1957, **79**, 1005; 1958, **80**, 6098; Smith, Marx, Garbarini, Foell, Origoni, and Goodman, *ibid.*, 1960, **82**, 4619.

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show that equatorial protons absorb at lower fields than axial protons (average difference *ca.* 0·3 p.p.m.[14]) and that absorption bands due to axial protons are broader, owing to more pronounced axial–axial coupling patterns. Supplementary evidence is given by the nuclear magnetic resonance spectra of the acetates (III and IV; X = Ac).

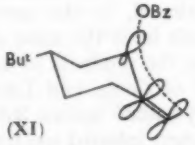
Infrared Spectra.—The strong absorption bands in the 900 cm.$^{-1}$ region associated with the compounds containing an exocyclic methylene group are tabulated. A small but distinct shift to higher frequencies is observed for compounds with α-oxygenated substituents. Thus an equatorial α-substituent causes a shift of 4—9 cm.$^{-1}$ and an axial α-substituent a somewhat larger shift of 15—20 cm.$^{-1}$. The markedly reduced ε values noted for some α-substituted methylenic compounds, where free rotation about the =C–CX– bond can occur,[15] were not observed with these more rigid systems.

Infrared absorption bands in the 900 *cm.*$^{-1}$ *region.*

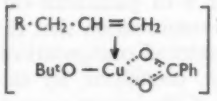
		X = H		X = CO·$C_6H_3(NO_2)_2$		X = Ac	
Compound	I	IV	III	IV	III	IV	III
Band (cm.$^{-1}$)	890	894	905	899	910	894	909

Discussion.—The major allylic substitution product from the reaction of t-butyl perbenzoate with 1-methylene-4-t-butylcyclohexane is therefore the benzoate (III; X = Bz) with an axial benzoyloxy-group. The epimeric benzoate is only formed to a minor extent.

A free-radical mechanism could explain this result. Thus abstraction, by a t-butoxy-radical, of an axial rather than an equatorial α-hydrogen atom should be facilitated by the favourable overlap of the π-orbitals of the double bond with the developing *p*-orbital containing the odd electron. Conversely, on combination of the allylic radical so formed with a benzoyloxy-radical, a stereoelectronic preference for axial insertion would be expected (cf. XI). This situation would thus be the free-radical counterpart of the ionic bromination of cyclohexanones which, under suitable conditions, gives the axial α-bromo-cyclohexanone.[16]



(XI)



(XII)

If, on the other hand, an intermediate complex of the type proposed by Denney, Denney, and Feig [3] (cf. XII) is involved in the t-butyl perbenzoate reaction, then the stereochemical outcome may be determined by the preferred direction of co-ordination of the olefin with the copper complex. In the case of the methylene hydrocarbon (I) co-ordination of the copper complex from the side *trans* to the t-butyl group would direct attack on to the axial hydrogen atom at $C_{(2)}$ [or $C_{(6)}$]. That attack in this sense by a bulky metal complex might be expected is indicated by the reaction of the methylene hydrocarbon (I) with osmium tetroxide, which gives solely the product resulting from attack *trans* to the t-butyl group.[17] A clear decision awaits sharper delineation of the mechanism of the t-butyl perbenzoate reaction. For the present it seems that the presence of small amounts of the equatorial allylic substitution product favours the second alternative. On this basis it could result from co-ordination to a small extent from the less favoured side.

[14] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, London, 1959, p. 116.
[15] Barton, de Mayo, and Shafiq, *J.*, 1958, 3314.
[16] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.
[17] Cross and Whitham, unpublished results.

Experimental

For general remarks see Part I.[4]

2-Methylene-trans-*5-t-butylcyclohexanol* (III; X = H).—(*a*) To 1-methylene-4-t-butylcyclohexane (5·2 g.) in dry benzene (600 c.c.) were added cuprous chloride (0·15 g.) and t-butyl perbenzoate (15·4 g.), and the mixture was heated under reflux during 8 hr. [In preliminary experiments the decomposition of t-butyl perbenzoate in benzene at the above concentration in the presence of cuprous chloride was followed by the disappearance of the 1755 cm.$^{-1}$ infrared band (per-ester). After 8 hr. all the per-ester had decomposed, the products being biphenyl, benzoic acid, and t-butyl alcohol.] The mixture was filtered and washed with water. Removal of benzene gave a syrup which was hydrolysed with 20% methanolic potassium hydroxide at 20° under nitrogen during 48 hr. The neutral fraction was obtained as an oil which was chromatographed on alumina. Elution with light petroleum gave biphenyl (1·41 g.), m. p. 69—70°. Further elution with light petroleum–ether (1 : 1) and (1 : 9) gave an oil (1·67 g.) which was rechromatographed. Elution with light petroleum–ether (8 : 2) and (7 : 3) gave the trans-*alcohol* (1·45 g., 26%), b. p. 116—118°/12 mm., n_D^{20} 1·4805, m. p. *ca.* 25° (Found: C, 78·5; H, 11·5. $C_{11}H_{20}O$ requires C, 78·5; H, 12·0%), $\lambda_{max.}$ 3580, 1086, 1041, 1018, 983 (OH), 3060, 1650, 905 (C=CH_2), 1369 cm.$^{-1}$ (Bu^t). Continued elution with light petroleum–ether (6 : 4) gave an oil (0·25 g.). The infrared spectrum of the latter exhibited, in addition to bands due to the *trans*-alcohol, bands at 1089, 1075, 1055, and 894 cm.$^{-1}$ shown later to be characteristic of the *cis*-alcohol (IV; X = H).

Further elution of the original column with ether gave hydroxy-compounds showing no exocyclic methylene absorption in the infrared spectrum.

(*b*) Crude product from the reaction of t-butyl perbenzoate (0·9 g.) with 1-methylene-4-t-butylcyclohexane (0·34 g.) was dissolved in dry ether (10 c.c.), lithium aluminium hydride was added, and the mixture was heated under reflux during 1 hr. Decomposition with water was followed by treatment with aqueous sodium potassium tartrate. Isolation with ether gave an oil which was chromatographed on alumina. Elution with light petroleum gave material (0·16 g.) which was not further investigated; further elution with light petroleum–ether (97 : 3) and (9 : 1) gave an oil (63 mg.) shown by its infrared spectrum to be identical with the *trans*-alcohol obtained as under (*a*).

2-Methylene-trans-*5-t-butylcyclohexyl 3,5-Dinitrobenzoate*.—3,5-Dinitrobenzoyl chloride (3·03 g.) in dry benzene (60 c.c.) was added at 0° to the *trans*-alcohol (III; X = H) (1·14 g.) in dry benzene (20 c.c.) containing dry pyridine (0·94 g.) and left at 8° during 12 hr. Pyridine hydrochloride was filtered off and the benzene layer was washed with aqueous sodium carbonate and water. Evaporation of the dried solution followed by chromatography of the residue in benzene on alumina gave the *3,5-dinitrobenzoate* (300 mg.), m. p. 78—80° (from ethanol) raised to 84—85° after two further recrystallisations (Found: C, 59·55; H, 5·8. $C_{18}H_{22}N_2O_6$ requires C, 59·65; H, 6·1%).

2-Methylene-cis-*5-t-butylcyclohexanol* (IV; X = H).—3-t-Butylcyclohexanone[10] (15·6 g.) was added to a suspension of dry sodium methoxide (from sodium, 4 g.) in dry benzene (150 c.c.) under nitrogen. Ethyl formate (16 g.) was added and the mixture was shaken and set aside at 20° for 12 hr. Iced water was added and the aqueous layer was collected. The benzene layer was washed with cold aqueous sodium hydroxide (5 × 50 c.c.), and all the aqueous layers were combined, washed once with ether, and acidified with dilute hydrochloric acid. After addition of salt, isolation with ether gave the 2-hydroxymethylene-5-t-butylcyclohexanone (11·5 g.), b. p. 94—98°/1 mm.

The hydroxymethylene-ketone (11·5 g.) in ether was added to a stirred suspension of lithium aluminium hydride (4 g.) in dry ether (200 c.c.), and the mixture was heated under reflux for 1 hr. After addition of water and sodium potassium tartrate the product was iolated with ether. Distillation gave an oil (5·5 g.), the infrared spectrum of which had a band at 1685 cm.$^{-1}$ (αβ-unsaturated ketone), presumably due to the presence of some ketone (V). The oil was accordingly resubmitted to the reduction sequence with lithium aluminium hydride (1 g.). Isolation as before followed by chromatography on alumina gave the *alcohol* (3·7 g., 33%), b. p. 74°/0·4 mm., n_D^{19} 1·4855, m. p. *ca.* 20° (Found: C, 78·0; H, 11·85%). $\nu_{max.}$ 3560, 1087, 1073, 1054 (OH), 3060, 1650, 894 (C=CH_2), and 1367 cm.$^{-1}$ (Bu^t). The *3,5-dinitrobenzoate*, formed as above in 44% yield, was obtained as needles, m. p. 153·5—154°, from light petroleum (b. p. 80—100°)

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(Found: C, 59·65; H, 6·45%). The *acetate* had b. p. 65—66°/0·2 mm., n_D^{21} 1·4659 (Found: C, 74·3; H, 10·65. $C_{13}H_{22}O_2$ requires C, 74·25; H, 10·55%).

2-Methyl-5-t-butylcyclohexanone (VIII).—(*a*) Palladium–carbon (10 mg.) was added to 2-methylene-*cis*-5-t-butylcyclohexanol (120 mg.) in methanol (8 c.c.), and the mixture was heated under reflux during 2 hr. After filtration, evaporation of the filtrate gave an oil which was chromatographed on alumina (activity I). Elution with light petroleum–ether (98 : 2) and (95 : 5) gave the ketone (60 mg.) as an oil, $\nu_{max.}$ (in CCl_4) 1723 cm.$^{-1}$ (C=O). The *2,4-dinitrophenylhydrazone* formed orange prisms (from ethanol), m. p. 169—170° (Found: C, 58·8; H, 7·0; N, 16·0. $C_{17}H_{24}N_4O_4$ requires C, 58·6; H, 6·95; N, 16·1%).

(*b*) 2-Methylene-*trans*-5-t-butylcyclohexanol (100 mg.) was similarly treated with palladium–carbon to give the methyl ketone (25 mg.). Its infrared spectrum was rich in detail and was identical with that of the ketone obtained as under (*a*). The 2,4-dinitrophenylhydrazone had m. p. undepressed on admixture with that prepared above.

Ozonolysis of 2-Methylene-5-t-butylcyclohexyl 3,5-Dinitrobenzoates.—Ozonised oxygen was bubbled through a solution of the *cis*-derivative (94 mg.) in methylene dichloride (2 c.c.) containing pyridine (28 mg.) at −75°. After 10 min. reaction was shown to have ceased by the liberation of iodine from acidic potassium iodide solution by the exit gases. The solution was warmed to 25°, washed with water, saturated aqueous cadmium chloride, and dried. Evaporation followed by crystallisation from methanol gave the *2-(3,5-dinitrobenzoyloxy)-cis-4-t-butylcyclohexanone* (64 mg.) as needles, m. p. 165—166° (Found: C, 56·05; H, 5·7; N, 7·5. $C_{17}H_{20}N_2O_7$ requires C, 56·05; H, 5·55; N, 7·7%).

The *trans*-derivative (150 mg.), ozonised in the same way, gave a gum (120 mg.). A portion (50 mg.) was heated in a 0·1N-solution of perchloric acid in aqueous acetone for 40 min. Addition of water followed by isolation with ether gave material (35 mg.) which crystallised on trituration with methanol and after two recrystallisations from methanol had m. p. 163—165° undepressed on admixture with a sample from the previous preparation. The infrared spectra were identical.

Nuclear Magnetic Resonance.—Spectra were measured on a Mullard instrument at 32 mcycles/sec. in carbon tetrachloride with tetramethylsilane as internal reference. Peak positions are in cycles/sec. from tetramethylsilane = 0.

We thank Professor M. Stacey, F.R.S., for encouragement, and Dr. L. F. Thomas for the nuclear magnetic resonance data. One of us (B. C.) thanks the D.S.I.R. for a maintenance grant.

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[*Received, October 20th,* 1960.]

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322. *The Biosynthesis of Polyacetylenes. Part III.* Polyacetylenes and Triterpenes in* Polyporus anthracophilus.

By J. D. BU'LOCK, D. C. ALLPORT, and W. B. TURNER.

The matricaria ester (I) which occurs in *P. anthracophilus* is derived from acetate by head-to-tail linkage. The polyacetylenes in this species are in a dynamic state, with synthesis *de novo* accompanying their disappearance. The incorporation of acetate into triterpenes proceeds simultaneously and may be very efficient; in different strains of the fungus competition between triterpene and polyacetylene synthesis is apparent.

OVER a hundred polyacetylenes have been isolated from two principal sources—plants (Compositae) and higher fungi (Agaricales).[1] Each type of source generally affords a distinctive variety of polyacetylene, but members of the important C_{10} group have been found in both plants and fungi. It seems probable, on structural grounds, that all the

* Part II, Bu'Lock and Gregory, *Biochem. J.*, 1959, **72**, 322.

[1] Reviewed by Jones, *Proc. Chem. Soc.*, 1960, 199.

known polyacetylenes have similar biogenetic origins, and in a search for useful parallels to the experimentally demonstrated derivation of nemotinic acid from acetate [2] the biogenesis of the matricaria ester (I) seemed an appropriate subject, since stereoisomers of the ester (I) occur frequently in Compositae [3] and in certain Basidiomycetes. Moreover, the fungus *Polyporus anthracophilus* Cke, from which *trans-trans*-ester (I) was first isolated [4] has a complex metabolism which itself seemed to merit further study.

In extracts from surface cultures of *P. anthracophilus* made at various times, at least 17 polyacetylenes, have been detected, of which 13 have been characterised, all but one being C_{10} substances with oxygen groups at one or both ends of the molecule. Besides

$CH_3 \cdot CH{=}CH \cdot C{\equiv}C \cdot C{\equiv}C \cdot CH{=}CH \cdot CO_2Me$ (I)

$CH_3 \cdot CH{=}CH \cdot C{\equiv}C \cdot C{\equiv}C \cdot CH{=}CH \cdot CH_2 \cdot OH$ (II)

$HO \cdot CH_2 \cdot CH_2 \cdot C{\equiv}C \cdot C{\equiv}C \cdot CH{=}CH \cdot CO_2Me$ (III)

$HO_2C \cdot CH{=}CH \cdot C{\equiv}C \cdot C{\equiv}C \cdot CH{=}CH \cdot CO_2H$ (IV)

matricaria ester (I), the major metabolites are the alcohol (II), the hydroxy-ester (III), and the diacid (IV) (and its diester). The proportions of these components vary as the cultures develop.[4]

FIG. 1. *Production of the major metabolites* (I—III) *from quantitative analyses of successive flasks. The full curves show the general trends found in* 1956 *and* 1959, *the broken curves the detailed effects found only in* 1956.

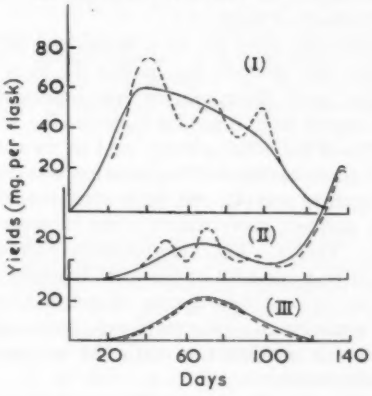
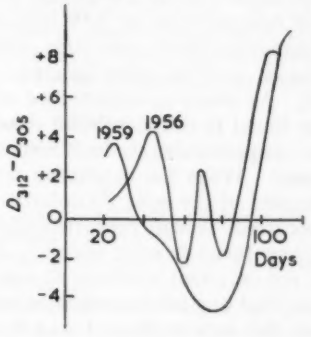


FIG. 2. *Relative amounts of products* (II) *and* (III) *in the aqueous medium of single flasks, from the optical-density difference, showing typical results from the* 1956 *and* 1959 *series.*



These variations have now been examined in more detail by two methods, with complementary results. In the first, samples of the medium from a given flask were examined spectroscopically, giving a qualitative picture not affected by uncontrolled differences between flasks. In the second, the entire contents of successive culture-flasks were analysed quantitatively by multi-component spectroscopic assay; the accuracy of this assay is limited, and moreover to follow the sequence of changes the data from different flasks must be used; the agreement between the two sets of data is, however, significant.

In all polyacetylene-producing strains of *P. anthracophilus* the same general picture was found, shown in the full curves of Fig. 1. The matricaria ester (I) predominates during growth of the cultures and up to 15 weeks after inoculation, the alcohol (II) being present in smaller amounts. Both begin to disappear from the cultures after 5—9 weeks, but whereas the loss of the ester is continued, the amount of alcohol (II) suddenly increases

[2] Bu'Lock and Gregory, *Biochem. J.*, 1959, **72**, 322.
[3] Sörensen, *Chem. and Ind.*, 1953, 240.
[4] Bu'Lock, Jones, and Turner, *J.*, 1957, 1607.

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sharply, reaches a rather high level, and then finally disappears. This pattern was shown by parent strains in 1956 and by descendant strains three years later. However, with the 1956 strains more complex variations were superimposed on this general pattern.

In the aqueous culture medium, the concentration of esters (I) soon reaches the solubility limit, and thereafter the main changes are in the proportions of compounds (II) and (III); since these have their longest-wavelength absorption maxima at 312 and 305 mμ respectively, the difference between optical densities at these wavelengths is a qualitative index of the relative amounts present. In the 1956 experiments, successive measurements on contents of the same flask consistently showed marked fluctuations, with the alcohol (II) and the hydroxy-ester (III) predominating alternately, in addition to the general phenomena already described (cf. Fig. 2). After allowance for uncertainties the full analyses for three series of flasks containing the same strains confirmed this unusual picture, and, as shown by the broken lines in Fig. 1, the fluctuations involved both the matricaria ester (I) and the alcohol (II), whereas the concentration of the hydroxy-ester (III) varied more simply; the latter observation proves incidentally that the apparent variations as regards components (I) and (II) are not due to the analytical method. With descendant strains, in 1959, these quasi-periodic short-term variations were not observed, as shown by the qualitative data in Fig. 2; the alcohol (II) predominated over the hydroxy-ester (III) in the early and the late phase, but was a minor component in the intermediate phase. The intimate mechanism of these fluctuations, and the related question of our failing to reproduce them at will, are beyond the scope of present information, but all the observations show clearly that in *P. anthracophilis* the polyacetylenes are not merely inert products but are also broken down and synthesised anew.

The incorporation of [1-^{14}C]acetate into matricaria ester (I) by a strain not showing the short-term effects was next studied. When the acetate was added 27 days after inoculation and the ester isolated 7 days later, good incorporation was observed (see Table). As would be expected for a C_{10} chain formed from 5 similar C_2 units, $C_{(1)}$ of ester (I) was found to contain almost exactly one-fifth of the total activity and in view of the earlier comprehensive study of nemotinic acid [2] no more detailed degradation was deemed necessary. When the incubation with [1-^{14}C]acetate was 42—63 days after inoculation the amount of the ester (I) isolated was much smaller; nevertheless some incorporation had occurred, though proportionally much less (Table). The incorporation represented strictly synthesis *de novo*, since $C_{(1)}$ still acquired just one-fifth of the total labelling; this shows not only that synthesis *de novo* of the ester (I) continues during its net destruction, but also that any interconversions which occur amongst the polyacetylenes, such as might explain the data of Figs. 1 and 2, do not involve equilibration with the symmetrical substances such as (IV) which are simultaneously present.

By incubation at a still later period incorporation into the alcohol (II) was to be studied, but with these cultures the phase when this alcohol predominates was rather short and, on working up, no polyacetylenes could be isolated (Table).

Incorporation of [1-^{14}C]*acetate into matricaria ester.*

Flasks	^{14}C added (days from inoculation)	Worked up (days from inoculation)	Triterpenes (mg.)	^{14}C in triterpenes (%)	Ester (I) (mg.)	^{14}C in (I) (%)	Proportion of ^{14}C in $C_{(1)}$ of (I)
1, 2	27	35	500	41	56	6·0	1·01/5
3, 4	42	63	570	7·0	22	0·2	1·01/5
5, 6	96	108	370	7·2	1	0·1	—

The stock cultures available to us differed, not only in detailed aspects of polyacetylene synthesis, but also in their overall capacity to produce such compounds, some indeed having quite lost this capacity of the parent strain. It was, moreover, observed that these " defective " strains produced conspicuously larger amounts of eburicoic acid, the major triterpene of this species.[5] Thus, for example, the parent (1956) strain afforded after

[5] Gascoigne, Holker, Ralph, and Robertson, *J.*, 1951, 2346.

63 days *ca.* 120 mg. of triterpenes and *ca.* 110 mg. of matricaria ester (I) per flask, whilst the strain used in 1959 for the tracer experiments produced, again after 63 days, *ca.* 280 mg. of triterpenes and only 29 mg. of the ester (I). As shown in the Table, the triterpenes appear most rapidly during the earlier incubation, with extremely high acetate incorporation (41%), but appreciable synthesis persists for much longer. The triterpenes are known to be formed from acetate by a pathway diverging at an early stage from that which leads to fatty acids and (probably) polyacetylenes; somewhat similar cases of reciprocity between triterpene and fatty acid synthesis are well known for moulds.[6]

Experimental

Culture Conditions.—Inocula were taken from subcultures of the parent strain, Forest Products Laboratory No. 327, made at 6-monthly intervals from 1956 to 1959 and stored under mineral oil at 4°, after plating-out on malt agar. The fungus was grown as surface cultures of 230 cm.^{2} on 700 ml. of glucose–salts–cornsteep medium supported on washed glass wool.

Analysis.—(a) *By repeated sampling.* Samples (10 ml.) were taken every 3—7 days from the aqueous medium of individual flasks in a batch of ten or twelve, some flasks being used only at the beginning or end of the series to minimise the effect of depletion by sampling; the samples were equilibrated with equal volumes of ethyl acetate or methylene dichloride, and the extracts examined spectroscopically between 250 and 360 mμ.

(b) *By total extraction.* Pairs of flasks were taken at weekly intervals from a large batch; the mycelium and medium were separated and each was extracted exhaustively with ether. The combined extracts were washed with aqueous sodium hydrogen carbonate to remove small amounts of acids, and then diluted with ethanol for spectroscopic examination. If D_{332}, D_{312}, D_{305} are optical densities at 332, 312, and 305 mμ respectively, then for a mixture of products (I), (II), and (III) in amounts W_1, W_2, W_3 mg. in V ml. of extract, calculations from measured absorption spectra of the pure components and mixture of known composition give that

$$W_1 = \tfrac{1}{2}V(11{\cdot}09D_{332} - 0{\cdot}664D_{312} + 0{\cdot}09D_{305})$$
$$W_2 = \tfrac{1}{2}V(8{\cdot}77D_{312} - 2{\cdot}93D_{305} - 7{\cdot}38D_{332})$$
$$W_3 = \tfrac{1}{2}V(11{\cdot}55D_{305} - 8{\cdot}15D_{332} - 3{\cdot}32D_{312})$$

With known mixtures these equations give W_1 and W_3 within ±5%, W_2 within ±10%, the uncertainty arising mainly from the steepness of the absorption curves.

(c) *General.* The results in the Figures are typical of those obtained in several experiments, *e.g.*, three for each curve in Fig. 1, eight for the curves of Fig. 2.

Incorporation of [1-^{14}C]*Acetate.*—To each of two culture-flasks in a batch of six, prepared as above, [1-^{14}C]acetate was added as the sodium salt (70—100 μc) at the time shown in the Table; 7—20 days later (cf. Table) the contents of the two flasks were removed and worked up as previously described,[4] by ether-extraction and chromatography on alumina. The triterpene fraction (eburicoic and dehydroeburicoic acid [5]) was washed free from fats by benzene and ether before counting. The matricaria ester (I) was weighed (22—56 mg.) and purified by recrystallisation with pure inactive material (220 mg.) and chromatography on alumina. Part of the product (*ca.* 50 mg.) was hydrogenated in light petroleum over 10% palladium–strontium carbonate, and the hydrogenation product saponified with ethanolic potassium hydroxide to give an oil (37 mg.) which was diluted with inactive hexanoic acid (270 mg.) before reversed-phase chromatography,[7] giving the purified hexanoic acid (249 mg.). Part of the purified acid (39 mg.) was converted by way of the acid chloride into the *p*-bromoanilide, m. p. 105—106°, purified by recrystallisation to constant activity. Another portion (27 mg.) was degraded by the Schmidt reaction,[8] giving barium carbonate from $C_{(1)}$. Radiochemical methods were as described previously,[9] and the results are summarised in the Table.

The University, Manchester, 13. [*Received, November 3rd,* 1960.]

[6] See, *e.g.*, Prill, Wenck, and Peterson, *Biochem. J.*, 1935, **29**, 21.
[7] Crombie, Comber, and Boatman, *Biochem. J.*, 1955, **59**, 309.
[8] Blomstrand, *Acta Chem. Scand.*, 1954, **8**, 1487.
[9] Allport and Bu'Lock, *J.*, 1960, 654.

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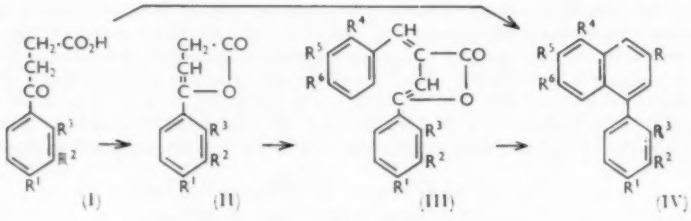
323. β-*Aroyl-α-arylmethylenepropionic Acids. Part II.* The Synthesis and the Mechanism of Isomerisation of their Enol Lactones.*

By Lanson S. El-Assal, and (Mrs.) Awatef H. Shehab.

β-Aroylpropionic acids or their sodium salts are converted by warm acetic anhydride into the corresponding lactones (II) which condense with aromatic aldehydes to give the corresponding α-arylmethylene-lactones (III) (Perkin's conditions). Isomerisation of those of the latter lactones that have a *m*-alkoxyaryl group on the α-methylene-radical, to give the corresponding phenylnaphthalenes, supports the mechanism suggested previously.

Borsche [1] suggested that condensation of aromatic aldehydes with β-aroylpropionic acids (I) or their sodium salts at the α-position, to give β-aroyl-α-arylmethylenepropionic acid lactones (III), occurred by intermediate formation of the γ-aryl-crotonolactones (II) derived from enol forms, and Hag *et al.*[2] isolated one such lactone (IId). The aims of the present work were to isolate several such lactones, convert them under the conditions of the original condensation into lactones (III), and, thereby, to study the effect of substituents on the mode of their isomerisation to 4-phenyl-2-naphthoic acids (IV).



(I) (II) (III) (IV)

I, II)

	R^1	R^2	R^3		R^1	R^2	R^3
a	H	H	H	d	OMe	OMe	H
b	OMe	H	H	e	Cl	H	H
c	Me	H	H	f	H	H	OMe

(III, IV)

	R_1	R_2	R_3	R_4	R_5	R_6		R_1	R_2	R_3	R_4	R_5	R_6
a	OMe	H	H	H	H	H	k	OMe	OMe	H	H	$-O\cdot CH_2\cdot O-$	
b	OMe	H	H	OMe	H	H	l	OMe	OMe	H	H	OMe	H
c	OMe	H	H	H	OMe	H	m	H	H	H	H	OMe	H
d	OMe	H	H	H	H	OMe	n	Cl	H	H	H	OMe	H
e	OMe	H	H	H	OMe	OMe	o	Me	H	H	H	OMe	H
f	OMe	H	H	H	$-O\cdot CH_2\cdot O-$		p	H	H	OMe	H	OMe	H
g	Me	H	H	H	OMe	OMe	q	Cl	H	H	H	$-O\cdot CH_2\cdot O-$	
h	Me	H	H	H	$-O\cdot CH_2\cdot O-$		r	H	H	H	H	$-O\cdot CH_2\cdot O-$	
i	Me	H	H	H	H	H	s	H	H	H	H	NO_2	H
j	OMe	OMe	H	H	OMe	OMe							

When the aroylpropionic acids (Ib, c, and d) or their sodium salts were gradually heated to 70—80° in acetic anhydride, the corresponding lactones (IIb, c, and d) were obtained in 90—95% yield [3,4] (see Table 1). Heating at 100° alone gave oils and resins at the expense of the yield and purity of the lactones, perhaps owing to preferential interaction of the produced enol-form of the acids and the acetic anhydride at high temperatures. Heating the acids (Ib, c, and d) at about 20° above their melting points also

* Part I, *J.*, 1959, 1020.

[1] Borsche, *Ber.*, 1914, **47**, 1108.
[2] Hag, Kapur, and Ray, *J.*, 1933, 1087.
[3] Fittig and Ginsberg, *Annalen*, 1898, **299**, 11, 18.
[4] Kugel, *Annalen*, 1898, **299**, 54.

produced the lactones, but less well. The structure of these lactones was confirmed by their infrared stretching frequencies 1800 ± 2 cm.$^{-1}$ characteristic of βγ-unsaturated lactones [5] (see Table 1).

The lactones (IIb, c, and d) condensed readily when heated with aromatic aldehydes (Perkin's conditions), to give the corresponding lactones (III) in satisfactory yields (see Table 2). Heating above 100° [1,2] gave inferior purity and yield.

These results place beyond doubt the mechanism suggested by Borsche.[1] The reactivity of the α-methylene group under the effect of the neighbouring polarised carbonyl group has now been assessed by such condensations.

The lactones (IIIb, c, and k—s) were prepared by the present method in satisfactory yields, and isomerised to pure 4-phenyl-2-naphthoic acids (IV; R = CO_2H) in boiling glacial acetic and concentrated hydrochloric acid [6] (see Table 4), the results being better than those of others.[6] Since the crude acids were pure (m. p. only 1—2° low), we believe the possibility of attachment at $C_{(2)}$ to be greatly diminished by steric factors.

Decarboxylation of the naphthoic acids (IVb, c, and k—s; R = CO_2H) with copper-bronze in quinoline gave the corresponding 1-phenylnaphthalenes (IV; R = H) (see Table 6). 6-Methoxy-1-phenyl- (IVm; R = H) and -1-*p*-tolyl-naphthalene (IVc; R = H) gave oils that were identified as the crystalline nitro-derivatives. Dechlorination [6] of 1-*p*-chlorophenyl-6-methoxy- (IVn; R = H), and -6,7-methylenedioxy-naphthalene (IVq; R = H) by palladised charcoal in tetralin at 205—210° yielded 6-methoxy- and 6,7-methylenedioxy-1-phenylnaphthalene, whose nitro-derivatives were identical with those obtained from the decarboxylation products of acids (IVm and r; R = CO_2H). This showed that isomerisation of the lactones (IIIm, n, q, and r) occurred by attachment at the same position 6 of their α-arylmethylene radical, independently on the nature of the *para*-substituent in the β-aroyl radical. The structures of five of the 1-phenylnaphthalenes were established by identity with authentic specimens.[7]

The successful isomerisation of lactones (IIIk, q, and r) in which the 3,4-positions are occupied by electron-repelling groups supports our previous observation.[6] However, the reaction of lactones (IIIc, k, l, m, n, and o), which have only *one* electron-repelling group in the *meta*-position of their α-arylmethylene radical, proves that the only effective factor is this electron-repelling group independently of the nature and position of the substituents in the β-aroyl-radical (see Table 4). This was supported by the failure of the lactones (IIIb and s) to isomerise (see Part I [6] for further examples).

We believe that isomerisation of the lactones of type (III) by hydrogen chloride in glacial acetic acid is initiated by attack of the proton on the lactone-oxygen atom, the C–O bond gradually weakening until heterolysis sets in. As a result, the partial positive charge developed at the γ-carbon atom attacks the centre which is made electronegative by the electron-repelling substituent R[5] (as in electrophilic substitution) and so leads to formation of 4-phenyl-2-naphthoic acids (IV; R = CO_2H).

Experimental

Microanalyses were by Dr. A. Bernhardt, Mikroanalytisches Laboratorium im Max-Planck-Institut, Mulheim (Ruhr), Germany.

Preparation of 4-*Aryl*-4-*hydroxybut*-3-*enoic Acid Lactones* (II).—*Method* (i). The β-aroylpropionic acid (I) (*ca.* 2 g.) was heated in acetic anhydride (4—5 ml.) to 70—80° during 2 hr., kept thereat for a further 3 hr., then left overnight at 20—25°. The precipitate was filtered off, washed with dry light petroleum (b. p. <40°), and crystallised from light petroleum (b. p. 60—70°), to give the *lactones* (II) in light or reddish-brown flakes which depress the m. p. of their parent acids.

[5] Cf. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co. Ltd., London, 1956, p. 153.
[6] El-Assal and Shehab, *J.*, 1959, 1020.
[7] El-Assal and Shehab, unpublished work.

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Hag *et al.*[2] obtained the lactone (IId) in yellow silky needles (from hot water), m. p. 114—115° (contrast Table 1; colourless with faint blue tint), and we believe that their compound is a dilactone or an anhydride.[3,4]

Infrared measurements were carried in Nujol mull for the lactones (IIb and c) and in chloroform for the lactone (IId) by the use of Infracord model 137 (Perkin–Elmer).

Method (ii). β-Aroylpropionic acids (I) were heated about 20° above their m. p. (oil-bath) for 3—4 hr., cooled, and extracted with dry light petroleum (b. p. 60—80°). On concentration

TABLE 1. *Lactones* (II).

	M. p.	Yield (%)	$\nu_{max.}$ (cm.$^{-1}$)	Found (%) C	H	OMe	Formula	Required (%) C	H	OMe
IIb	103—104°	93	1798	69·7	5·25	16·6	$C_{11}H_{10}O_3$	69·5	5·3	16·3
IIc	92—93	95	1800	75·5	5·8	—	$C_{11}H_{10}O_2$	75·9	5·75	—
IId	94—95	92	1802	65·7	5·7	28·9	$C_{12}H_{12}O_4$	65·45	5·45	28·2

TABLE 2. *Lactones* (III).

Lactone (III)	From lactone (II)	Solvent *	Colour	M. p.	Yield (%)	Ref.
a	IIb	C_6H_6	Greenish-yellow	176—177°	90	*a*
b	IIb	AcOH	Reddish-brown	164—165	60	†
c	IIb	AcOH	Yellowish-green	157—158	75	†
d	IIb	AcOH	Greenish-yellow	177—178	85	6
e	IIb	AcOH	Orange-yellow	174—175	92	6
f	IIb	C_6H_6–Pet	Yellow	211—212	85	6
g	IIc	AcOH	Orange	144—145	90	6
h	IIc	$CHCl_3$	Orange	214—215	98	6
i	IIc	C_6H_6–Pet	Yellow	133—134	65	1
j	IId	Aq. AcOH	Green	148—150	92	*b*
k	IId	Ac_2O	Golden-yellow	228—229	93	†
	IId	AcOH	Greenish-brown	143—144	89	†

Lactone (III)	Found (%) C	H	OMe	Formula	Calcd. (%) C	H	OMe
a	77·6	5·1	11·6	$C_{18}H_{14}O_3$	77·7	5·0	11·15
b	74·3	5·3	19·7	$C_{19}H_{16}O_4$	74·0	5·2	20·1
c	73·6	5·0	19·9	$C_{19}H_{16}O_4$	74·0	5·2	20·1
d	74·3	5·25	19·6	$C_{19}H_{16}O_4$	74·0	5·2	20·1
e	71·3	5·5	27·0	$C_{20}H_{18}O_5$	71·0	5·3	27·5
f	71·2	4·5	9·1	$C_{19}H_{14}O_5$	70·8	4·35	9·6
g	74·2	5·65	19·65	$C_{20}H_{16}O_4$	74·5	5·6	19·25
h	74·7	4·7	—	$C_{19}H_{14}O_4$	74·5	4·6	—
i	82·6	5·2	—	$C_{18}H_{14}O_2$	82·4	5·3	—
j	68·8	5·5	33·1	$C_{21}H_{20}O_6$	68·5	5·4	33·7
k	68·4	4·6	17·2	$C_{20}H_{16}O_5$	68·2	4·55	17·6
l	71·4	5·15	28·0	$C_{20}H_{18}O_5$	71·0	5·3	27·5

* Pet. = Light petroleum (b. p. 60—70°). † These lactones were identical with those prepared by the modified direct method (ii) in this investigation (see Table 3).
a, Howell and Robertson, *J.*, 1936, 587. *b*, Haworth and Sheldrick, *J.*, 1935, 636.

and repeated crystallisation from the same solvent, the products gave the lactones (II) but in much lower yield than for method (i).

The lactones (IIb, c, and d) are insoluble in cold sodium hydrogen carbonate and 5% sodium carbonate solution but dissolve in hot or boiling alkali solution to give the parent acids (identical m. p. and mixed m. p.s); the lactone ring breaks on storage with exposure to moisture or in boiling with water (several minutes) (contrast Hag *et al.*[2]).

Preparation of 4-Aryl-2-arylmethylene-4-hydroxybut-3-enoic Acid Lactones (III).—*Two-step method* (i). A mixture of the aromatic aldehyde (1·2 mol.), 4-aryl-4-hydroxybut-3-enoic acid lactone (1 mol.), and sodium acetate (1 mol.) in acetic anhydride (2 mol.) was heated to 70—80° during 2 hr., kept thereat for a further 5 hr., and left overnight at 20—25°. The precipitate was filtered off, washed with water, dried, and recrystallised. The products, lactones (III), were identical with those described in the literature and those prepared by the modified method of this investigation (identical m. p. and mixed m. p.) (see Table 2).

Isomerisation of the lactone (IIIj) by our method gave 4-(3,4-dimethoxyphenyl)-6,7-dimethoxy-2-naphthoic acid (IVj; R = CO_2H), which on decarboxylation with copper-bronze in quinoline gave 1-(3,4-dimethoxyphenyl)-6,7-dimethoxynaphthalene [8] (IVj; R = H).

Modified direct method (ii). A mixture of β-aroylpropionic acid (I) or its sodium salt (1 mol.), aromatic aldehyde (1·2 mol.), and sodium acetate (1 mol.) in acetic anhydride (6 mol.) was heated to 60—80° during 2 hr., kept thereat for a further 4 hr., left overnight at 25—30°, and worked up in the usual manner.[6] The product, on crystallisation from acetic acid, gave the β-aroyl-α-arylmethylenepropionic acid lactones (III) described in Table 3.

Isomerisation of Lactones (III) *to 4-Phenyl-2-naphthoic Acids* (IV; R = CO_2H).—The lactone (III) (1 g.) was refluxed in glacial acetic and concentrated hydrochloric acid (1 : 1 v/v) (50 ml.) for 2—6 hr. (see Table 4) (to disappearance of the lactone colour) and then left to cool. The precipitate was filtered off, washed with water, and digested in sodium carbonate solution,

TABLE 3. *Lactones* (III) *prepared by method* (ii).

Lactone (III)	From acid (I)	and benzaldehyde	Colour	M. p.	Yield (%)
b	b	*o*-Methoxy-	Yellowish-brown	159—160°	50
c	b	*m*-Methoxy	Yellowish-green	159—160	75
k	a	3,4-Methylenedioxy-	Yellow	175—176	50
l	d	*m*-Methoxy-	Green	144—145	86
m	a	*m*-Methoxy-	Orange-yellow	117—118	76
n	e	*m*-Methoxy-	Yellow	171—172	60
o	c	*m*-Methoxy-	Bright-red	152—153	60
p	f	*m*-Methoxy-	Yellow	143—144	50
q	e	3,4-Methylenedioxy-	Yellow	255—256	65
r	d	3,4-Methylenedioxy-	Golden-yellow	228—229	95
s	a	*m*-Nitro-	Yellowish-brown	204—205	50

Lactone	Found (%)					Required (%)			
(III)	C	H	OMe	Cl or N	Formula	C	H	OMe	Cl or N
b	74·3	5·15	19·8	—	$C_{19}H_{16}O_4$	74·0	5·2	20·1	—
c	73·6	5·1	19·9	—	$C_{19}H_{16}O_4$	74·0	5·2	20·1	—
k	73·6	4·2	—	—	$C_{18}H_{12}O_4$	74	4·1	—	—
l	70·5	5·2	26·9	—	$C_{20}H_{18}O_5$	71·0	5·3	27·5	—
m	77·6	5·1	11·2	—	$C_{18}H_{14}O_2$	77·7	5·0	11·15	—
n	69·1	4·4	9·7	11·0	$C_{18}H_{13}ClO_3$	69·1	4·2	9·9	11·4
o	77·6	5·5	9·3	—	$C_{19}H_{16}O_3$	78·1	5·5	10·6	—
p	73·5	5·3	19·8	—	$C_{19}H_{16}O_4$	74·0	5·2	20·1	—
q	65·9	3·5	—	9·8	$C_{18}H_{11}ClO_4$	66·15	3·4	—	10·9
r	68·2	4·6	17·4	—	$C_{20}H_{16}O_6$	68·2	4·55	17·6	—
s	69·2	3·95	—	5·0	$C_{17}H_{11}NO_4$	69·6	3·75	—	4·8

TABLE 4. *Production of 4-phenyl-2-naphthoic acids* (IV) *from the lactones* (III)

Reaction	Acid (IV;		Yield	Found (%)				Required (%)		
(hr.)	R = CO_2H)	M. p.	(%)	C	H	OMe	Formula	C	H	OMe
3	c	224—225°	100	74·0	5·1	19·9	$C_{19}H_{16}O_4$	74·0	5·2	20·1
5	k	277—278	95	73·3	4·4	—	$C_{18}H_{12}O_4$	74	4·2	—
6	l	192—193	100	70·65	5·1	27·4	$C_{20}H_{18}O_5$	71·0	5·3	27·5
3·5	m	199—200	89	77·1	4·8	11·1	$C_{18}H_{14}O_2$	77·7	5·0	11·15
3	n	215—216	100	69·3	4·3	10·1	$C_{18}H_{13}ClO_3$ *	69·1	4·1	9·9
1·5	o	221—222	96	77·8	5·6	11·1	$C_{19}H_{16}O_3$	78·1	5·5	10·8
6	p	254—255	90	73·5	5·2	21·3	$C_{19}H_{16}O_4$	74·0	5·2	20·2
3	q	265—266	100	66·2	3·6	10·4	$C_{18}H_{11}ClO_4$ †	66·15	3·4	10·9
1·5	r	266—267	89	67·8	4·6	16·7	$C_{20}H_{16}O_6$	68·2	4·55	17·6

* Found: Cl, 10·4. Reqd.: Cl, 11·0%. † Found: Cl, 10·4. Reqd.: Cl, 10·9%.

and the insoluble product (traces) was removed. Acidification of the clear alkaline filtrates (charcoal) precipitated acids which on crystallisation from acetic acid gave nearly colourless crystals of the 4-phenyl-2-naphthoic acids (IV; R = CO_2H), described in Table 4. The acids were best analysed after esterification and recovery by hydrolysis.

[8] Haworth and Sheldrick, *J.*, 1935, 636.

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Some of the sodium salts of these acids were insoluble in cold water; these were filtered off and reconverted into the acids which were dried in a vacuum at 90—100° before analysis.

The methyl esters (Table 5) were prepared by means of methanol–sulphuric acid, diazomethane, or methyl sulphate–potassium carbonate in acetone, and recrystallised from methanol or benzene–light petroleum (b. p. 60—70°).

1-*Phenylnaphthalenes* (IV; R = H).—A stirred mixture of an acid (IV; R = CO_2H) (*ca.* 0·5 g.) and copper-bronze (0·25 g.) in quinoline (10 ml.) was heated to the b. p. during 30 min. More copper-bronze (0·25 g.) was added in portions during 90 min. with continued stirring and heating. The mixture was cooled, poured into dilute hydrochloric acid, and repeatedly extracted with ether. Working up the extract in the usual way gave a residue which solidified on trituration with warm light petroleum (b. p. <40°) and crystallised to give the 1-phenylnaphthalene (IV; R = H) in light-brown crystals (see Table 6) which did not depress the m. p. of the authentic specimen.[7] Yields were 70—80%.

6-Methoxy-1-phenyl- (IVm; R = H), and -1-*p*-tolyl-naphthalene (IVo; R = H) were oils and were identified as their nitro-derivatives, which were prepared by means of nitric acid (*d* 1·42) in acetic acid at 25—30° (3·5 hr.). They had, respectively, m. p. 147—148° (from acetic acid) (Found: C, 73·2; H, 4·6; OMe, 10·8; N, 5·15. $C_{17}H_{13}O_3N$ requires C, 73·1; H, 4·65; OMe, 11·1; N, 5·0%), and m. p. 143—145° [from light petroleum (b. p. 60—70°)] (Found: C, 73·5; H, 5·2; OMe, 10·65; N, 5·0. $C_{18}H_{15}O_3N$ requires C, 73·0; H, 5·1; OMe, 10·6; N, 4·75%).

TABLE 5. *Methyl 4-phenyl-2-naphthoates* (IV; R = CO_2Me).

		Found (%)					Required (%)			
Ester	M. p.	C	H	OMe	Cl	Formula	C	H	OMe	Cl
c	103—104°	74·5	5·55	28·3	—	$C_{20}H_{16}O_4$	74·5	5·6	28·9	—
k	170—171	74·3	4·6	10·5	—	$C_{19}H_{14}O_4$	74·5	4·6	10·1	—
l	138—139	71·4	5·75	34·8	—	$C_{21}H_{20}O_5$	71·3	5·7	35·2	—
m	77—78	78·2	5·6	21·05	—	$C_{19}H_{16}O_3$	78·1	5·5	21·2	—
n	130—131	69·7	4·8	18·4	10·5	$C_{19}H_{15}ClO_3$	69·8	4·6	18·7	10·9
o	93—94	78·1	5·8	19·8	—	$C_{20}H_{18}O_3$	78·4	5·9	20·3	—
p	155—156	74·1	5·4	29·3	—	$C_{20}H_{16}O_4$	74·5	5·6	28·9	—
q	166—167	66·55	3·9	9·7	9·15	$C_{19}H_{12}ClO_4$	66·95	3·8	9·1	10·4
r	175—176	68·6	5·0	25·1	—	$C_{21}H_{16}O_6$	68·85	4·9	25·3	—

TABLE 6. 1-*Phenylnaphthalenes* (IV; R = H).

			Found (%)					Required (%)			
Compound	Solvent	M. p.	C	H	OMe	Cl	Formula	C	H	OMe	Cl
c	Pet.[a]	85—86°	81·5	6·1	22·15	—	$C_{18}H_{16}O_2$	81·8	6·0	23·5	—
k	MeOH	134—135	73·85	5·3	19·9	—	$C_{19}H_{16}O_4$	74·0	5·2	20·1	—
n	Pet[b]	72—74	75·8	4·8	11·4	13·6	$C_{17}H_{13}ClO$	76	4·8	11·5	13·2
q	MeOH	113—114	71·8	4·15	—	12·5	$C_{17}H_{11}ClO_2$	72·2	3·9	—	12·6
r	MeOH	87—88	82·4	5·0	—	—	$C_{17}H_{12}O_2$	82·25	4·8	—	—

[a, b] Light petroleum of b. p. (*a*) 60—70°, (*b*) 50—60°.

Dechlorination of 1-p-*Chlorophenyl-6-methoxynaphthalene* (IVn; R = H).—1-*p*-Chlorophenyl-6-methoxynaphthalene (0·15 g.), dry tetralin (0·5 ml.), and 10% palladised charcoal (0·6 g.) were heated at 205—210° until the evolution of hydrogen chloride stopped (*ca.* 4 hr.). The cooled product was extracted with boiling benzene. Removal of the solvent in a vacuum left 6-methoxy-1-phenylnaphthalene (*ca.* 0·1 g.) that was identified as its nitro-derivative, m. p. and mixed m. p. 147—148° (Found: C, 73·4; H, 4·5; OMe, 11·0; N, 4·9%).

1-*p*-Chlorophenyl-6,7-methylenedioxynaphthalene (IVq; R = H) (0·07 g.), tetralin (0·3 ml.), and 10% palladised charcoal (0·03 g.) similarly gave 6,7-methylenedioxy-1-phenylnaphthalene (IVr; R = H), m. p. and mixed m. p. 87—88° (from methanol) (Found: C, 82·3; H, 4·9%).

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324. *The Reaction of Dichloromethylene with Water and with Phenoxide Ions (Reimer–Tiemann Reaction).*

By Edwin A. Robinson.

The formation of dichloromethylene is already well established as the rate-controlling step in the alkaline hydrolysis of chloroform in aqueous solution. This investigation is concerned with the subsequent reactions which lead to the products, carbon monoxide and formate. Measurement of the ratio of these products during the course of the reaction at several initial hydroxide concentrations shows that carbon monoxide and formate are not formed simultaneously but that carbon monoxide is the primary product from which formate is produced by a subsequent slow reaction with hydroxide ions. These observations lead to a rate expression for the alkaline hydrolysis of chloroform different from that used hitherto.

Experiments based on competition with chloride ions have revealed that dichloromethylene reacts exclusively, or almost exclusively, with water and not with hydroxide ions. A mechanism for the formation of carbon monoxide is suggested.

The addition of phenoxide to the system results in competition between water and phenoxide ions for dichloromethylene. The relative rates at which substituted phenoxides react with dichloromethylene are consistent with what might be expected for electrophilic attack on these aromatic nuclei. This is believed to be the first kinetic evidence for the Reimer–Tiemann reaction and is in accord with a recently proposed mechanism.

The rate-determining step in the hydrolysis of chloroform by aqueous alkalis is the unimolecular elimination of a chloride ion from the trichloromethyl anion:[1]

$$CHCl_3 + OH^- \overset{\text{fast}}{\rightleftharpoons} H_2O + {}^-CCl_3 \quad . . . . . (1)$$

$${}^-CCl_3 \xrightarrow{\text{slow, } k_2} CCl_2 + Cl^- \quad . . . . . (2)$$

$$CCl_2 \xrightarrow{H_2O,\ OH^-} \text{products} \quad . . . . . (3)$$

Hine and his co-workers, as well as Fells and Moelwyn-Hughes,[2] have assumed that the ultimate products, carbon monoxide and formate, are formed from dichloromethylene by simultaneous reactions but this mechanism has not been established experimentally. If this assumption is correct then the ratio of products should remain approximately constant during the course of the reaction.

The concentration of each product has now been determined at intervals during the reaction. The results of runs for which several different initial hydroxide concentrations were used are plotted in Fig. 1 and illustrate clearly that the ratio of products ($H{\cdot}CO{\cdot}O^-/CO$) is very small soon after the reaction has commenced and that this ratio increases continuously as the reaction proceeds. This can only mean that carbon monoxide is the primary product of the decomposition of dichloromethylene. When the reaction is carried out in sealed tubes the concentration–time curves are typically those of consecutive reactions (Fig. 2). The rate of formation of formate (measured graphically) is proportional to the product of the concentrations of hydroxide and carbon monoxide; this is a rather slower reaction than the formation of dichloromethylene. Step (3) in the reaction scheme therefore includes the following consecutive reactions:

$$CCl_2 \xrightarrow{2OH^-,\ H_2O} CO \quad . . . . . (4)$$

$$CO \xrightarrow[k_5]{OH^- \text{ (slow)}} H{\cdot}CO{\cdot}O^- \quad . . . . . (5)$$

[1] Hine, *J. Amer. Chem. Soc.*, 1950, **72**, 2438 *et seq.*
[2] Fells and Moelwyn-Hughes, *J.*, 1959, 398.

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The Decomposition of Dichloromethylene in Aqueous Alkaline Solution.—The first step in the decomposition of dichloromethylene (4) may involve reaction with water or with hydroxide ions or with both. It is possible to distinguish between these alternatives by considering the following competitive reactions (cf. Hine and Dowell [3]):

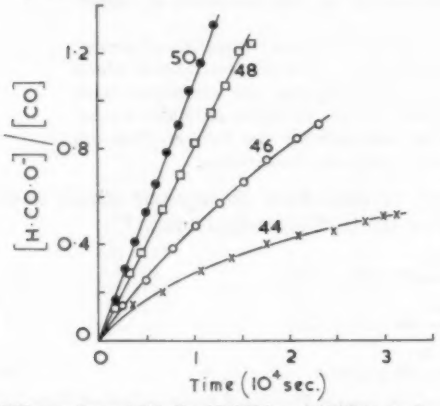
$$CCl_2 + H_2O \xrightarrow{k_w} CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$CCl_2 + OH^- \xrightarrow{k_h} CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$CCl_2 + Cl^- \xrightarrow{k_c} {}^-CCl_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

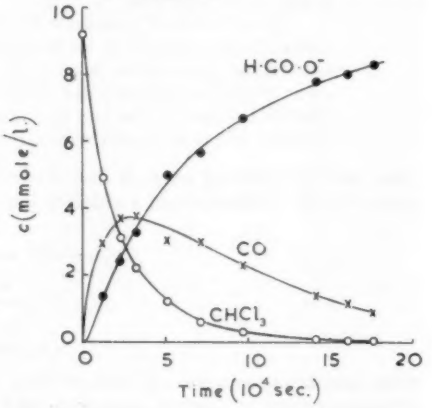
k_w, k_h, and k_c are first-order rate constants for the reactions between water, hydroxide, and chloride respectively and the common intermediate, dichloromethylene. The last

FIG. 1. *Change in the ratio of products during the hydrolysis of chloroform with aqueous sodium hydroxide at* 45·0°.



(All runs have, initially, $[CHCl_3] = 0{\cdot}01195$M, and [NaOH] is 0·0492M in run 44, 0·0968M in run 46, 0·1470M in run 48, and 0·1949M in run 50.)

FIG. 2. *Concentrations of reactant and products during the alkaline hydrolysis of chloroform in sealed tubes at* 45·0°.



reaction (8) is a reversal of the rate-determining step for the hydrolysis of chloroform and therefore reduces the overall rate of reaction. If it is assumed that all of these reactions occur, then the fraction of dichloromethylene which decomposes to carbon monoxide is represented by the right-hand side of equation (9) and this is also the fraction to which the initial rate constant (k_2^0) will be reduced by the addition of chloride. If $k_2^{0\prime}$ is the initial rate constant in the presence of added chloride, then

$$\frac{k_2^{0\prime}}{k_2^0} = \frac{[H_2O] + (k_h/k_w)[OH^-]}{[H_2O] + (k_h/k_w)[OH^-] + (k_c/k_w)[Cl^-]} \quad . \quad . \quad . \quad . \quad (9)$$

provided that the total ionic strength be kept constant by the addition (where necessary) of a salt which has a negligible effect on the rate of reaction. From the salts which are known to fulfil this condition,[3] sodium nitrate was chosen because of its relatively high solubility, a property which is necessary for the technique used here. The concentration terms in equation (9) are initial concentrations. In this expression both k_h/k_w and k_c/k_w should be constants. If, however, dichloromethylene is attacked by water only then, by similar arguments, the following equation should hold:

$$k_2^{0\prime}/k_2^0 = [H_2O]/([H_2O] + (k_c/k_w)[Cl^-]) \quad . \quad . \quad . \quad . \quad . \quad (10)$$

[3] Hine and Dowell, *J. Amer. Chem. Soc.*, 1954, **76**, 2688.

The third alternative, that dichloromethylene reacts exclusively with hydroxide ions, gives:

$$k_2^0/k_2^9 = [OH^-]/([OH^-] + (k_c/k_h)[Cl^-]) \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

If the initial rate constants are determined with sufficient accuracy at various initial concentrations of hydroxide ions in the presence and absence of added chloride, then the actual mode of decomposition of dichloromethylene should be distinguishable.

The rate expression for the alkaline hydrolysis of chloroform is

$$dx/dt = k_2(a - x)(b - y) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

where a and b are the initial concentrations of chloroform and hydroxide respectively and x and y are the corresponding changes in concentration. The hydrolysis of each molecule of chloroform requires three hydroxide ions, and one additional hydroxide ion is involved in the subsequent production of one formate ion. Therefore all values of y/x fall within the relatively narrow limits of **3** and **4**. At zero time dy/dx has the same value under all conditions (*i.e.*, **3**) and this is very nearly identical with the value of y/x in the early part of the reaction. As we are only concerned with initial rate constants, it appears to be permissible to assume that y/x is a constant for the purpose of integrating equation (12). Extrapolation of the rate coefficients, calculated from the integrated rate equation (13), to zero time should give the true initial rate constant (k_2^0). In fact, when the measured

$$\bar{k}_2 = \frac{2{\cdot}303}{t(b - ay/x)} \log \frac{a(b - y)}{b(a - x)} \quad . \quad . \quad . \quad . \quad . \quad (13)$$

values of x and of y are inserted in equation (13) the rate coefficient, $\bar{k}_2$, remains constant almost until the reaction is complete (Table 1).*

TABLE 1. *Integrated second-order rate coefficients ($\bar{k}_2$ in sec.$^{-1}$ mole^{-1} l.) obtained during the hydrolysis of chloroform in aqueous sodium hydroxide at 45·0° in tightly stoppered flasks.*

Run **4**: Initially, $[CHCl_3]$ = 0·0919M and [NaOH] = 0·05915M.

Time (sec.)	10,620	18,000	23,160	30,600	36,360	82,380
$\bar{k}_2$	11·6	11·7	11·6	11·7	11·6	11·6
Reactn. (%)	46·8	63·1	70·4	78·5	82·5	96·0

Run **10**: Initially, $[CHCl_3]$ = 0·00458M and [NaOH] = 0·05945M.

Time (sec.)	7860	15,480	20,280	25,620	30,900	36,060
$\bar{k}_2$	10·8	10·7	10·8	11·1	11·1	11·0
Reactn. (%)	38·0	59·1	68·8	76·9	82·5	86·2

Run **11**: Initially, $[CHCl_3]$ = 0·00457M and [NaOH] = 0·1068M.

Time (sec.)	3840	7080	11,040	14,580	17,340	20,340
$\bar{k}_2$	10·6	10·6	10·6	10·6	10·6	10·4
Reactn. (%)	34·6	53·5	69·0	78·3	83·2	87·2

However, not all of the results obtained by the technique used for the runs in Table 1 were so consistent, and discrepancies became more apparent when higher concentrations of reactants were used. Measurement of the pressure generated in the reaction vessels showed that it could be as high as 4 atm.; on releasing the spring-loaded stoppers it was obvious that some of these had failed to hold this pressure. Also, the rate of gas evolution, at atmospheric pressure, from the same reaction mixture under the same conditions varied from flask to flask; this may have been connected with the condition of the internal

* It is emphasised that although Hine [1] has used a different rate expression for k_2, the resulting inaccuracy of his rate constants is small enough not to affect his general conclusions concerning the mechanism for the alkaline hydrolysis of chloroform because in his tests the chloroform was always in excess and the constant small value which was assigned to y/x [$(3 + f)$ in his papers] merely displaced all values of k_2 to about the same extent.

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surface of each flask because the addition of powdered glass always increased the rate of gas evolution. Far more reliable results were obtained by taking all samples from the same vessel and maintaining the reaction mixture at atmospheric pressure. Under these conditions the loss of some chloroform vapour causes a decrease in the value of the rate coefficients as the reaction proceeds but as this decrease is related to the reaction time in an approximately linear manner there is no difficulty in extrapolating the rate coefficients to zero time (Fig. 3). The direct titration of formate in place of the titration of chloride further increases the accuracy of this method.

Some initial rate constants determined by this method are reported in Table 2. Substitution of these values in equations (9), (10), and (11) results in a constant value for

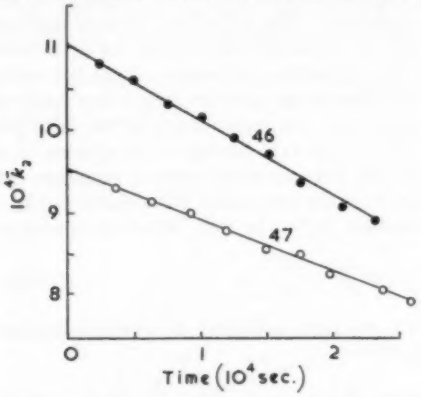


FIG. 3. *Extrapolation of $\bar{k}_2$ to k_2^0 for run 46 (no added chloride) and run 47 (with added chloride).*

k_c/k_w only in the case of equation (10). When the results are substituted in equation (9) a series of equations is obtained, each pair of which may be solved for k_h/k_w, *e.g.*:

$$\text{Runs 44 and 45 give } k_c/k_w = 44{\cdot}2 + 0{\cdot}0393k_h/k_w$$

$$\text{Runs 46 and 47 give } k_c/k_w = 43{\cdot}3 + 0{\cdot}0763k_h/k_w$$

hence from this pair of equations $k_h/k_w = 24$.

TABLE 2. *Relative rates of reaction of water and chloride ions with dichloromethylene at 45·00°.*

$[CHCl_3]_0 = 0{\cdot}01195$M. $\mu = 0{\cdot}40$.
Initial rate constants for the hydrolysis of chloroform (k_2^0 and $k_2^{0\prime}$) in sec.$^{-1}$ mole^{-1} l.
Second-order rate constant for the formation of formate (k_2) = $(d[H{\cdot}CO{\cdot}O^-]/dt)/[CO]_a[OH^-]$ in sec.$^{-1}$ mole^{-1} l., $[CO]_a$ being the molar concentration of carbon monoxide in solution.

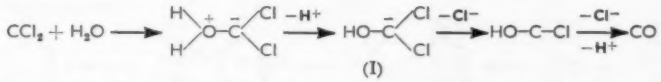
Run	$[NaOH]_0$	$[NaCl]_0$	$10^4k_2^0$	$10^4k_2^{0\prime}$	k_c/k_w †	10^4k_2
44	0·0492	nil	10·85	—	45·5	7·85 ± 0·55
45	0·0489	0·20	—	9·35		8·25 ± 0·35
46	0·0968	nil	11·05	—	43·0	8·3 ± 0·3
47	0·0974	0·20	—	9·55		7·8 ± 0·65
48	0·1470	nil	11·25	—	44·7	8·45 ± 0·35
49	0·1471	0·20	—	9·7		7·9 ± 0·2
50	0·1949	nil	11·25	—	43·8	8·0 ± 0·5
51	0·1948	0·20	—	9·7		8·2 ± 0·2
52 ‡	0·0970	0·10	—	10·25	43·6	8·75 ± 0·45
53 ‡	0·0977	0·30	—	8·9	43·9	8·2 ± 0·2

† Calculated from equation (10). ‡ Paired with Run 46.

The values of k_h/k_w which are obtained from all of the possible pairs of equations are: 24, 1·3, 0·9, 33, −5, −19, −10, 0, −26, 8, −14, 4, the mean being −0·2. The maximum error in the determination of the initial rate constants is about 0·5%, but even such a small error has a pronounced effect on the calculated value of k_h/k_w; *e.g.*, if the value of $10^4k_2^0$ for run 44 were 10·80 instead of 10·85 the value of k_h/k_w in the example above would

change from +24 to −15. These small experimental errors should be largely cancelled out when all possible pairs of simultaneous equations are taken into account, and the fact that the mean value of k_h/k_w from these equations is very nearly zero indicates either that the reaction between dichloromethylene and hydroxide ions does not occur at all or, if it does occur, that it is kinetically insignificant. Thus the first step in the decomposition of dichloromethylene to carbon monoxide involves reaction with water and not with hydroxide ions to any discernible extent. Dichloromethylene is believed to have a non-linear singlet structure and to possess considerable carbonium-ion character.[4] The observed reluctance of dichloromethylene to react with hydroxide ions may at first appear surprising, but in fact this behaviour is quite consistent with that of carbonium ions of comparable stability, *e.g.*, the diphenylmethyl carbonium ion.[5]

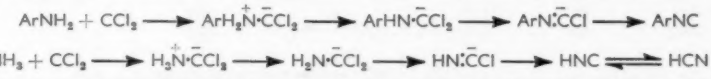
On the present evidence the most likely mechanism for the decomposition of dichloromethylene to carbon monoxide is:-



(I)

It may be noted that (I) is not likely to lose a proton before a chloride ion is eliminated because carbonyl chloride would be formed, and under these conditions this would hydrolyse to carbonate, a product which has not been detected in this reaction.

Certain nucleophilic reagents, other than water, probably react with dichloromethylene in an analogous manner; *e.g.*, in the presence of chloroform and aqueous alkalis, primary aromatic amines yield aryl isocyanides,[6] and ammonia yields hydrogen cyanide:[7]



The Reaction between Carbon Monoxide and Aqueous Alkalis.—The subsequent reactions in which formate is produced from carbon monoxide and aqueous alkali would be difficult to study directly at atmospheric pressure because of the low solubility of carbon monoxide in water. Under the present conditions, however, the gas is generated *in situ* and highly supersaturated solutions are formed; *e.g.*, the maximum concentration of carbon monoxide in solution in Run 40 was 14 times greater than the normal solubility under these conditions. These concentrations were sufficiently large for a kinetic investigation to be attempted.

The rate constant for the decomposition of carbon monoxide to formate can be calculated from

$$k_3 = (\mathrm{d}[\mathrm{H{\cdot}CO{\cdot}O^-}]/\mathrm{d}t)/[\mathrm{OH^-}][\mathrm{CO}]_s \quad . \quad . \quad . \quad . \quad . \quad (14)$$

where $[CO]_s$ is as defined in Table 2. This involves a graphical determination of the rate of formate formation and has a relatively large error. The results for k_3 in Tables 2 and 3

TABLE 3. *Effect of the alkali cation on the rate of formation of dichloromethylene and of formate at 45·00° (k_2^0 and k_3 in sec.$^{-1}$ mole^{-1} l.).*

Run	Alkali	$[CHCl_3]_0$	$10^4k_2^0$	10^4k_3
39	0·0957M-NaOH	0·01195	11·5	8·1 ± 0·3
40	0·0471M ,,	0·0359	11·6	8·15 ± 0·25
41	0·0475M ,,	0·01195	11·2	7·7 ± 0·35
42	0·0463M-KOH	0·0359	12·1	8·4 ± 1·25
43	0·0972M ,,	0·01195	12·1	7·8 ± 0·45

are the mean values for the points in the middle of the runs where the tangents could be measured with greater accuracy. These results embrace a 30-fold change in the ratio

[4] Skell and Garner, *J. Amer. Chem. Soc.*, 1956, **78**, 5430; Doering and Henderson, *ibid.*, 1958, **80**, 5274; Hine and Ehrenson, *ibid.*, p. 824.
[5] Benfey, Hughes, and Ingold, *J.*, 1952, 2494.
[6] Hofmann, *Annalen*, 1868, **146**, 109.
[7] Sidgwick, " The Organic Chemistry of Nitrogen," Oxford, 1937, p. 304.

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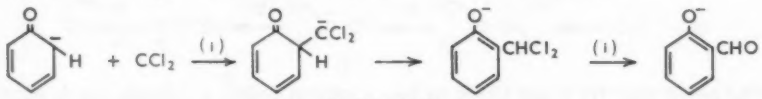
of concentrations of hydroxide and carbon monoxide in solution. The approximate constancy of k_3 confirms that the formation of formate from carbon monoxide and hydroxide ions follows second-order kinetics and this, in addition to the absence of any large salt effects, suggests that the mechanism involves a direct slow attack by hydroxide ions on the carbon atom in carbon monoxide followed by a prototropic rearrangement to formate. Such a mechanism has already been proposed by Christiansen and Galdbach.[8] The higher rate of formation of dichloromethylene in the presence of potassium cations confirms previous observations; it has been suggested that the smaller tendency of potassium than of sodium to form ion pairs with the trichloromethyl anion may increase the rate of chloride elimination from this anion.[3]

The Reimer–Tiemann Reaction.—The foregoing observations suggested a method by which the kinetics of a more complex related reaction might be studied. Wynberg [9] has suggested the following mechanism for the Reimer–Tiemann reaction:



If this sequence of reactions is correct then, because it has now been shown that hydroxide ions do not react with dichloromethylene to any appreciable extent, the first step in this sequence must involve competition between water and phenoxide ions for dichloromethylene to form carbon monoxide and hydroxy-aldehydes respectively:

$$CCl_2 + H_2O \xrightarrow{k_w} CO$$

$$CCl_2 + PhO^- \xrightarrow{k_p} \text{hydroxy-aldehydes}$$

If F is the proportion of dichloromethylene which reacts to give aldehydes, and k_w and k_p represent first-order rate constants, then at constant ionic strength,

$$F = [PhO^-]/([PhO^-] + (k_w/k_p)[H_2O]) \quad . \quad . \quad . \quad . \quad . \quad (15)$$

It would be difficult to determine small changes in the concentration of phenoxide in the presence of phenolic aldehydes. It has therefore been assumed that the change in phenoxide concentration is equal to the concentration of aldehydes formed. This assumption is probably justified at the relatively low concentrations used; the only other major products of the Reimer–Tiemann reaction (from phenols which do not carry *ortho*- or *para*-alkyl substituents) are resins, and there was no obvious sign of resin formation on acidifying the reaction mixtures in the tests reported here. This assumption being allowed, equation (15) may be written as

$$\frac{k_p}{k_w} = \frac{[\text{Aldehydes}][H_2O]}{[PhO^-]_{av.}(\Delta[CHCl_3] - [\text{Aldehydes}])} \quad . \quad . \quad . \quad . \quad (16)$$

The use of the average phenoxide concentration is permissible because in no case is the change in phenoxide concentration greater than 8·5%.

The competition factors (k_p/k_w) reported in Table 4 are reasonably constant at different initial phenoxide and hydroxide concentrations. Moreover, the relative rates at which these various phenoxides react with dichloromethylene are in the order which might have been predicted from a consideration of the relative electron densities at the reaction sites in the aromatic nuclei. These results also show that carbon monoxide is not involved in the formation of the aldehydes, for if it were, then the ratio [aldehyde]/$\Delta[CHCl_3]$ should increase appreciably with the time of reaction as does the ratio $[H{\cdot}CO{\cdot}O^-]/\Delta[CHCl_3]$ in

[8] Christiansen and Galdbach, *Kgl. danske Videnskab. Selskab, Mat.-fys. Medd.*, 1942, **20**, No. 3.
[9] Wynberg, *J. Amer. Chem. Soc.*, 1954, **76**, 4998.

TABLE 4. *Relative rates of reaction of water and phenoxide ions with dichloromethylene at 45·0°.*

$[CHCl_3]_0$ = 0·0288M for tests 1—6 and 13—27.
$[CHCl_3]_0$ = 0·0450M for tests 9—12. μ = 0·40 for all tests.

Test	Phenol	Time (min.)	$[NaOH]_0$	$[Phenol]_0$	$10^4[Ald]_t$	$10^4\Delta[CHCl_3]$	k_p/k_w	Mean
1	Phenol	30	0·200	0·050	7·7	88	106	
2	,,	90	,,	,,	14·5	173·5	102	
3	,,	169	,,	,,	17·65	219·5	98·5	
4	,,	300	0·050	0·200	29·45	110·5	101	
5	,,	1380	,,	,,	42·6	164	97·5	102
6	,,	180	0·100	0·100	23·05	147·5	103·5	
9	,,	60	0·200	0·050	20·3	236·5	105·5	
10	,,	120	,,	,,	27·4	314·5	108	
11	,,	180	0·050	0·200	32·5	125·5	97	
12	,,	318	,,	,,	39·85	152	99	
13	4-Methoxyphenol	60	0·2055	0·039	10·25	142	112	
14	,,	180	,,	,,	15·45	223·5	107·5	
15	,,	300	,,	,,	16·8	249·5	104·5	110
16	,,	60	0·0829	0·1465	16·85	73·5	113	
17	,,	180	,,	,,	30·35	134	111·5	
18	,,	300	,,	,,	36·9	164·5	110·5	
19	Guaiacol	60	0·2055	0·039	12·9	142	144	
20	,,	180	,,	,,	19·4	225	137·5	
21	,,	300	,,	,,	22·05	257	137	
22	,,	60	0·0829	0·1465	19·9	74	140	140
23	,,	180	,,	,,	36·5	135·5	141	
24	,,	305	,,	,,	44·8	167	140·5	
25	2-Naphthol	60	0·1937	0·0485	25·0	140·5	254	
26	,,	180	,,	,,	38·95	223	251·5	251
27	,,	300	,,	,,	42·1	245	248	

the absence of phenoxides; in fact the ratio of aldehyde concentration to the change in chloroform concentration remains almost constant.

Thus the suggestion that the Reimer–Tiemann reaction proceeds by an electrophilic attack on the phenoxide nucleus by dichloromethylene is supported by these data.

EXPERIMENTAL

Materials.—" AnalaR " chloroform was purified just before use.[10] Benzene was refluxed for 6 hr. with an aqueous solution of sodium carbonate and potassium permanganate and then dried (Na_2SO_4) and distilled. All other materials were of " AnalaR " grade.

Analyses.—Initial chloroform concentrations were determined by a method which was developed for this investigation and which depends on the fact that chloroform in aqueous solution is hydrolysed completely by 3·5N-potassium hydroxide at 20° in 6 hr. Special precautions are necessary to prevent loss of chloroform vapour during transference of solutions and during hydrolysis. Full details of the procedure are published elsewhere.[11] Hydroxide was determined by running the sample into an excess of standard acid and back-titrating, phenolphthalein being used as indicator. For those runs which were performed in closed vessels, the neutral solution from the hydroxide titration was acidified with two drops of 4N-nitric acid and an excess of standard silver nitrate was added; after separation of the silver chloride the solution was titrated with thiocyanate using ferric alum indicator; the presence of phenolphthalein does not interfere with the determination of chloride. Formate was determined (in runs 39—53) by the following procedure. The sample was run into an excess of standard acid and neutralised by adding the volume of standard alkali which was required for the hydroxide determination. Sodium acetate was added, and the solution was extracted twice with benzene and then boiled to remove traces of benzene. An excess of standard permanganate was run from a burette into the hot solution which was then kept in a boiling-water bath for 5 min., acidified with sulphuric acid, and cleared with standard oxalic acid. The excess of oxalic acid was titrated with permanganate from the same burette.

[10] Fieser, " Experiments in Organic Chemistry," D. C. Heath & Co. Inc., New York, 1955, p. 283.
[11] Robinson, *Analyt. Chim. Acta*, 1960, **23**, 305.

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Procedure for runs in stoppered flasks. The reaction vessels were specially made 100 ml. volumetric Pyrex flasks with the graduation mark about 1 cm. below the stopper. The small vapour space in these flasks effectively reduced the loss of chloroform and carbon monoxide from the solution. The stoppers were spring-loaded. Chloroform solution at 45° was transferred under pressure into the appropriate volume of alkali solution at 45° contained in each of eight such flasks which were then stoppered and inverted twelve times to mix the contents. The whole contents of the last flask filled were poured immediately into an excess of acid for the initial hydroxide and chloride determinations. The water-bath used for these, and all other runs, was accurate to $\pm 0{\cdot}01°$ at 45° over a period of two weeks.

Procedure for run 5 (in sealed tubes). The alkali and chloroform solutions were mixed at 0°, and transferred under pressure to Pyrex tubes which were sealed immediately and immersed in the water-bath at 45°; 50 ml. aliquot parts were used for the titrations.

Procedure for runs 39—53. 200 ml. of alkali solution at 45° were added to 800 ml. of chloroform solution (of pre-determined concentration) at 45° in a 1 l. flask. After the solutions had been mixed, four 25 ml. samples were taken immediately and the flask was connected to a gas burette. Gas burette readings and gas temperatures were recorded frequently, and pairs of samples were taken at appropriate intervals. The time at which each sample was run into the excess of acid was recorded; the titres at zero time were determined graphically. The gas burette readings were corrected for chloroform vapour and for the expansion of air which displaced the samples by using a series of correction curves which were constructed from tests in which the hydroxide was omitted but for which the same sampling procedure was followed. The gas " blank " obtained from these curves depends on the duration of the interval between consecutive samples and the average concentration of chloroform in solution during this interval. A continuous curve for the evolution of carbon monoxide was obtained by extrapolating back over the sampling intervals. The carbon monoxide evolved, $[CO]_e$, for each point in a run corresponds to the mid-point of the sampling interval. The carbon monoxide in solution, $[CO]_s$, was calculated from:

$$[CO]_s = \Delta[CHCl_3] - [H{\cdot}CO{\cdot}O^-] - [CO]_e$$

Data for a sample run (39) are given below.

Initially, [NaOH] = 0·0957M and $[CHCl_3]$ = 0·01195M. Sample pipette = 25·00 ml. Initial volume = 1006 ml. Analytical solutions: NaOH = 0·0978N, $KMnO_4$ = 0·02534N. Gas measurements at 16° and 729 mm.; $\bar{k}_2$ and k_2 in sec.$^{-1}$ mole^{-1} l. $d[H{\cdot}CO{\cdot}O^-]/dt$ measured graphically in sec.$^{-1}$ l.$^{-1}$ mole.

Time (sec.)	Change in NaOH titre (ml.)	Change in $KMnO_4$ titre (ml.)	$10^4\bar{k}_2$	Vol. increase between samples (c.c.)	Gas blank (c.c.)	CO during sampling interval † (c.c.)
						0·25
2280	2·00	0·54	11·3	3·05	2·2	0·6
5040	3·76	1·78	11·0	8·0	1·6	1·05
7620	4·96	2·90	10·75	9·8	1·4	1·3
9900	5·82	4·02	10·6	9·6	1·15	1·15
12,600	6·58	5·08	10·35	9·4	1·2	1·5
14,580	7·05	5·64	10·25	8·0	0·95	1·15
17,160	7·54	6·40	10·0	7·9	1·05	1·05
19,860	7·95	7·24	9·65	7·0	1·0	0·8
22,260	8·25	7·71	9·45	4·5	0·9	0·5

Time (sec.)	CO at S.T.P. at mid-point of sampling interval (c.c.) †	$10^4[CO]_e$	$10^4[CO]_s$	$10^3 d[H{\cdot}CO{\cdot}O^-]/dt$	10^4k_2
2280	1·35	0·6	21·8	—	—
5040	8·85	3·9	33·1	—	—
7620	19·35	8·6	36·5	2·32	8·35
9900	30·6	13·7	34·9	2·06	8·1
12,600	42·3	18·9	32·7	1·79	7·85
14,580	53·25	23·8	30·1	1·61	7·85
17,160	64·5	28·8	26·3	1·45	8·35
19,860	75·15	33·5	21·2	—	—
22,260	82·2	36·7	18·7	—	—

$k_2^0 = 11{\cdot}5 \times 10^{-4}$ sec.$^{-1}$ mole^{-1} l.
k_2 (Mean) $= 8{\cdot}1 \times 10^{-4}$ sec.$^{-1}$ mole^{-1} l.
† Evolution from one litre of solution.

Reimer–Tiemann Tests.—Analyses. Ordinary phenol was determined volumetrically.[12] The initial concentration of substituted phenols was calculated from the weight used. Aldehydes were determined gravimetrically;[13] when 2-naphthol was present it was necessary to add ethanol (free from aldehydes) to prevent precipitation of unchanged naphthol, and to wash the derivative with 25% aqueous ethanol. Chloride was determined by Volhard's method which was not affected by the presence of aldehydes and phenols except in the case of guaiacol which formed a reddish colour with the ferric indicator; here the acidified sample was extracted with benzene before addition of the silver nitrate.

Procedure. 20 ml. of solution, containing a pre-determined concentration of sodium hydroxide and of the phenol, at 45° were added to 79 ml. of water containing 0·25 ml. of chloroform (and sodium nitrate where necessary) at 45° and the mixture was made up to 100 ml. The flask was removed from the water-bath for only a few seconds to mix the contents. After an appropriate interval, two 25 ml. portions of the reaction mixture were withdrawn and run into an excess of nitric acid for the chloride determinations, and the remainder (including the drainings retained by the 25 ml. pipette) was washed into hydrochloric acid for the determination of aldehydes.

RESEARCH DEPARTMENT, ARTHUR R. DAVIS & CO., LTD.,
GRAFTON ROAD, CROYDON, SURREY. [*Received, August 8th*, 1960.]

[12] Scott, "Standard Methods of Chemical Analysis," D. van Nostrand Co. Inc., New York, 1939, Vol. II, p. 2253.
[13] Iddles and Jackson, *Ind. Eng. Chem. Analyt.*, 1934, **6**, 456.

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325. *Molecular Polarisability. Chloroform as a Solvent for the Determination of Molar Kerr Constants of Solutes.*

By R. J. W. LE FÈVRE and A. J. WILLIAMS.

The apparent values of the molar Kerr constants and dipole moments of two polar, and five ordinarily non-polar, solutes in chloroform are reported and considered in relation to the corresponding data obtained in carbon tetrachloride. Results suggest that chloroform has a limited usefulness for the estimation of principal polarisabilities of strongly polar species such as chloro- and nitro-benzene, but with other solutes, such as benzene, naphthalene, carbon disulphide, etc., unavoidable experimental errors are evidently liable to introduce unpredictable uncertainties in the interpretation of measurements by our usual methods of calculation.

THIS work originated with the question: can useful measurements of molar Kerr constants be made in polar media? It became necessary because the applicability of molecular polarisability [1] to stereochemistry was obviously limited while only solutions in non-polar media could be examined, since many interesting compounds are insoluble in such liquids. Chloroform was selected for test because of its satisfactory solvent powers for a wide range of substances. Our plan therefore has been to apply standard techniques to seven solutes in this solvent, and to compare results so secured with others already known from work with carbon tetrachloride, benzene, hexane, etc. The present paper logically follows that by Armstrong *et al.*,[2] which dealt with binary mixtures of non-polar components. Cases of polar solutes in non-polar solvents have previously been discussed by Le Fèvre and Le Fèvre [3] and by Buckingham.[4]

[1] Le Fèvre and Le Fèvre, *Rev. Pure Appl. Chem.*, 1955, **5**, 261.
[2] Armstrong, Aroney, Le Fèvre, Le Fèvre, and Smith, *J.*, 1958, 1474.
[3] Le Fèvre and Le Fèvre, *J.*, 1953, 4041; 1954, 1577; 1955, 2750.
[4] Buckingham, *Trans. Faraday Soc.*, 1956, **52**, 611.

Experimental

Materials, Apparatus, etc.—Solutes were dried and redistilled or recrystallised, as appropriate, immediately before their solutions were prepared. Bulk supplies of chloroform were at first treated as specified by Vogel.[5] Later, when the low electric birefringence of ethanol (commonly present in commercial chloroform) became known,[6] we found that 24 hours over calcium chloride followed by fractionation through a 1 m. column packed with glass helices produced a solvent satisfactory for present purposes. Apparatus already described [1,3,7,8] for measurements of Kerr effects and dielectric constants has been used without change except for minor alterations due to the electrical and optical properties of chloroform. Observations are listed in Table 1 under the headings: w_2, weight fractions; ε, dielectric constants; d, densities; and ΔB and Δn_D^2, increments in the Kerr constant and refractive index (Na light) from solvent to solutions. Subsequent calculations of apparent polarisations, moments, and molar Kerr constants at infinite dilution are given in Tables 2 and 3. Appropriate data for chloroform as a solvent at 25° and with $\lambda = 5893$ Å are: $\varepsilon = 4{\cdot}724$, $H = 2{\cdot}040$, ${}_sK_1 = -0{\cdot}1474 \times 10^{-12}$, $d = 1{\cdot}4790$, $J = 0{\cdot}2974$, $p_1 = 0{\cdot}37447$, $n_D = 1{\cdot}4430$, $B = -3{\cdot}22 \times 10^{-7}$, $C = 0{\cdot}04486$. These, and other symbols used later, are explained in ref. 1, p. 283, and ref. 8, p. 56.

Discussion

Observed Molar Kerr Constants.—In all cases except that of naphthalene the values of apparent ${}_\infty({}_mK_2)$ of Table 3 are algebraically lower than those obtained before [1,2,9] with carbon tetrachloride as solvent:

Solute	C_6H_6	C_6H_5Cl	$C_6H_5{\cdot}NO_2$	$C_{10}H_8$	$C_{14}H_{10}$	CS_2	CCl_4
${}_\infty({}_mK_2)_{CCl_4} \times 10^{12}$	7·2	145	1073	48·1	82·6	27·8	1·1
Reference	1	1	1	1	9	2	1
${}_\infty({}_mK_2)_{CHCl_3} \times 10^{12}$ ...	−5·2	101·5	744	51·4	71·0	17·0	−7·1

In ref. 2 it was demonstrated that a molecular polarisability semi-axis, as measured by experiment, appears to be influenced by the refractive index of the medium and by a " shape factor " k_i for the solute concerned; equations of the type

$$b_i^{soln}/b_i^{vapour} = 1 - K(n_1^2 - 1)(0{\cdot}333 - k_i)/(n_1^2 + 2)$$

(in which K could be 1, n_1, or n_1^2) were shown to represent this phenomenon adequately enough to forecast the variations of the molar Kerr constants of non-polar substances from solvent to solvent. Accordingly, since the refractive indexes of carbon tetrachloride and chloroform are about the same (1·4575 and 1·4430 respectively at 25°), so should be the semi-axes of a molecule dissolved in each of these liquids, provided the structure (shape) is similar in the two environments. As an initial step, therefore, we assume that the anisotropy term θ_1 (see ref. 1, p. 270, for definition) for a given solute in carbon tetrachloride is an acceptable approximation for the θ_1 of that solute when in chloroform.

The anisotropy terms for chloro- and nitro-benzene in carbon tetrachloride have been reported by Le Fèvre and Rao [10] as $4{\cdot}29 \times 10^{-35}$ and $5{\cdot}57 \times 10^{-35}$; from the present paper, and other details in ref. 10, it follows that the " dipole terms " θ_2 in the two media are in the ratios, for chlorobenzene $19{\cdot}9/30{\cdot}2 = 0{\cdot}66$, and for nitrobenzene, $171/250 = 0{\cdot}68$. According to Le Fèvre and Le Fèvre,[9] these ratios should resemble those for $\mu^2_{CHCl_3}/\mu^2_{CCl_4}$, which are 0·59 with chlorobenzene and 0·62 with nitrobenzene. Agreement is reasonable, in view of the nature of the measurements involved, and in accordance with the idea that apparent moments are much more strongly affected by the medium than are polarisability semi-axes.

[5] Vogel, " Practical Organic Chemistry," Longmans, Green & Co., London, 3rd edn., 1956, p. 176.
[6] Le Fèvre, Le Fèvre, Rao, and Williams, *J.*, 1960, 123.
[7] Buckingham, Chau, Freeman, Le Fèvre, Rao, and Tardif, *J.*, 1956, 1405.
[8] Le Fèvre, " Dipole Moments," Methuen, London, 3rd edn., 1953, p. 45.
[9] Le Fèvre and Le Fèvre, unpublished.
[10] Le Fèvre and Rao, *J.*, 1958, 1465.

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TABLE 1. *Kerr constants, refractivities, dielectric constants, and densities of solutions in chloroform containing weight fractions* w_2 *of solute at 25°.*

Solute: Benzene

10^5w_2	1468	3612	5647	5990	7108	7418	10,221	11,282	
d_4^{25}	1·4641	1·4429	1·4234	1·4200	1·4095	1·4067	1·3814	1·3718	
$10^4\Delta n_D$ ...	13	30	47	49	58	60	81	89	
10^5w_2	4064	4362	5445	5794	6555	6852	8640	9708	9757
ε^{25}	4·494	4·478	4·421	4·407	4·363	4·349	4·262	4·217	4·219
10^5w_2	11,251	12,296	15,151						
ε^{25}	4·147	4·105	3·991						

whence $\Delta\varepsilon = -5{\cdot}95w_2 + 7{\cdot}41w_2^2$; $\Delta d = -1{\cdot}023w_2 + 0{\cdot}65w_2^2$

10^5w_2	2948	3004	3051	4076	4581	4636	4774	4828	6154
$10^7\Delta B$ ...	0·218	0·197	0·328	0·404	0·425	0·430	0·403	0·393	0·527
$10^4\Delta n_D$ ...	—	—	24	34	—	—	—	—	—
10^5w_2	6267	6836	7741	8513	9125	9839	9884	13,545	21,030
$10^7\Delta B$ ...	0·567	0·654	0·665	0·735	0·780	0·835	0·767	—	—
$10^4\Delta n_D$ ...	52	—	62	—	—	—	—	105	160

whence $\Sigma(\Delta B \,.\, w_2)/\Sigma w_2^2 = +8{\cdot}59$; or $\Sigma\Delta B/\Sigma w_2 = +8{\cdot}65$; or $10^7\Delta B = +9{\cdot}511w_2 - 11{\cdot}98w_2^2$; and $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}0796$.

Solute: Chlorobenzene

10^5w_2	5299	5546	5950	6402	6578	7042	7062	7574
d_4^{25}	1·4530	1·4521	1·4502	1·4478	1·4472	1·4444	1·4447	1·4424
10^5w_2	8997	9427	12,031	12,714	12,984	13,725		
d_4^{25}	1·4360	1·4338	1·4218	1·4183	1·4177	1·4140		

whence $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}4811$

10^5w_2	5403	5781	8159	8170	9386	11,625	12,525	17,128
ε^{25}	4·791	4·795	4·821	4·821	4·836	4·863	4·876	4·926

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 1{\cdot}19_9$

10^5w_2	2151	2803	3229	3792	5302	5728	6068	6127	7176	8420	11,206
$10_4\Delta n_D$ ...	33	40	45	52	65	71	74	75	86	100	130

whence $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}1244$

10^5w_2	2113	3377	3863	5403	5781	6328	8170	9386
$10^7\Delta B$ ...	0·51	0·74	0·85	1·21	1·27	1·42	1·87	2·12

whence $\Sigma\Delta B/\Sigma w_2 = 22{\cdot}49$

Solute: Nitrobenzene

10^5w_2	682	1227	1388	1943	2021	2415	2597	2904
d_4^{25}	1·4770	1·4752	1·4746	1·4732	1·4729	—	1·4713	1·4703
$10^4\Delta n_D$ ...	10	15	18	23	24	35	33	37
10^5w_2	3483	4443	8126	9566	14,696			
d_4^{25}	1·4686	1·4657	1·4573	1·4534	1·4390			
$10^4\Delta n_D$ ...	56	58	113	134	200			

whence $\Delta d = -0{\cdot}291w_2 + 0{\cdot}15w_2^2$; $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}1363$

10^5w_2	1038	1523	2264	2283	2412	2919
ε^{25}	5·054	5·208	5·441	5·445	5·486	5·645

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 31{\cdot}6_3$

10^5w_2	261	290	412	539	548	594	663	697	794	872	892	1005	1175	1226
$10^7\Delta B$ ...	0·23	0·22	0·45	0·61	0·64	0·64	0·70	0·73	0·87	0·99	0·98	1·01	1·16	1·27

whence $\Sigma\Delta B/\Sigma w_2 = 105{\cdot}3$

Solute: Naphthalene

10^5w_2	1694	1776	2357	2953	3977	4009	6436	
d_4^{25}	1·4684	1·4679	1·4644	1·4607	1·4546	1·4544	1·4397	
10^5w_2	1612	2103	2935	3347	3426	4244	5151	5213
ε^{25}	4·654	4·632	4·596	4·578	4·576	4·540	4·504	4·501

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = -4{\cdot}30_6$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}6199$

10^5w_2	928	1143	1736	1769	2572	2754	2789	3315
$10^7\Delta B$ ...	0·131	0·209	0·319	0·316	0·436	0·472	0·510	0·525
$10^4\Delta n_D$ ...	22	29	45	46	68	71	70	88
10^5w_2	3506	3978	4053	5099	5532	6319	7952	
$10^7\Delta B$ ...	0·591	0·663	0·667	0·754	0·831	0·919	0·984	
$10^4\Delta n_D$ ...	91	103	106	132	139	161	170	

whence $\Sigma\Delta B/\Sigma w_2 = +16{\cdot}9_5$; or $\Sigma\Delta B \,.\, w_2/\Sigma w_2^2 = +16{\cdot}86$; and $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}2508$

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TABLE 1. (*Continued.*)

Solute: Phenanthrene

10^5w_2	548	1095	1434	1738	1789	1835	2136	2325	2392	2397	2648
d_4^{25}	1·4768	—	1·4729	1·4714	1·4714	1·4708	1·4699	—	1·4685	1·4687	1·4676
$10^4\Delta n_D$ ...	16	37	—	60	64	62	78	82	88	86	95
10^5w_2	3158	3270	3403	3578	3794	3996	4036	4784	4895	5437	5868
d_4^{25}	1·4649	1·4649	1·4641	1·4637	1·4623	1·4615	—	1·4581	1·4575	1·4553	1·4535
$10^4\Delta n_D$ ...	110	—	119	125	—	141	142	163	—	187	202
10^5w_2	2634	2845	4106	4954	5771	6220					
ε^{25}	4·633	4·626	4·583	4·552	4·524	4·514					

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = -3{\cdot}44$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}4365$; $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}2418$

10^5w_2	1020	1039	1428	1517	2464	2661	3505	3632	4349	5383
$10^7\Delta B$ ...	0·15	0·18	0·23	0·24	0·38	0·41	0·52	0·55	0·69	0·81

whence $\Sigma\Delta B/\Sigma w_2 = 15{\cdot}41$; or $\Sigma\Delta B \,.\, w_2/\Sigma w_2^2 = 15{\cdot}32$

Solute: Carbon disulphide

10^5w_2	3830	4140	7526	8444	9397	12,694
d_4^{25}	1·4675	1·4665	1·4567	1·4542	1·4513	1·4423
$10^4\Delta n_D$ ...	71	75	137	151	169	230
10^5w_2	2816	4375	4507	5721	8279	8567
ε^{25}	4·632	4·581	4·578	4·540	4·463	4·456

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = -3{\cdot}19_3$; $\Delta d = -0{\cdot}306w_2 + 0{\cdot}14w_2^2$

10^5w_2	927	1382	2226	2326	2657	3240	3319
$10^7\Delta B$ ...	—	0·238	0·261	0·291	—	0·400	0·378
$10^4\Delta n_D$ ...	18	24	39	41	50	58	59
10^5w_2	3737	4946	5835	6533	7419	7651	9349
$10^7\Delta B$ ...	0·444	0·565	0·645	0·750	0·859	0·828	1·062
$10^4\Delta n_D$ ...	68	88	105	119	132	130	165

whence $\Sigma\Delta B/\Sigma w_2 = 11{\cdot}60$; or $\Sigma\Delta B \,.\, w_2/\Sigma w_2^2 = 11{\cdot}40$; and $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}1793$

Solute: Carbon tetrachloride

10^5w_2	2508	2570	2738	3520	3555	3838	4249	5312	6543	6573
d_4^{25}	—	—	1·4818	—	—	1·4828	—	—	1·4854	—
$10^4\Delta n_D$ ...	4	3	3	4	4	4	6	6	7	7
10^5w_2	6644	7612	8479	8842	9537	10,089	13,366	14,891	16,456	
d_4^{25}	—	—	1·4873	—	1·4884	—	1·4921	—	—	
$10^4\Delta n_D$ ...	7	8	10	10	11	14	15	19	21	
10^5w_2	3176	5188	6370	8509	8717	11,294	14,786			
ε^{25}	4·631	4·575	4·539	4·482	4·474	4·406	4·308			

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = -2{\cdot}85$; $\Sigma\Delta d/\Sigma w_2 = +0{\cdot}0984$; and $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}0112$

10^5w_2	3094	4477	5434	5999	7213	7906	8568	9708	12,227	12,776
$10^7\Delta B$ ...	0·12	0·19	0·25	0·30	0·34	0·39	0·43	0·48	0·60	0·60
10^5w_2	14,745	15,873	17,427							
$10^7\Delta B$ ...	0·68	0·71	0·81							

whence $\Sigma\Delta B/\Sigma w_2 = -4{\cdot}70$; or $\Sigma\Delta B \,.\, w_2/\Sigma w_2^2 = -4{\cdot}69$

TABLE 2. *Total polarisations at infinite dilution, and apparent dipole moments, calculated from Table* 1.

Solute	$(\alpha\varepsilon_1)_{w_2=0}$	$(\beta)_{w_2=0}$	$_\infty P_2$ (c.c.)	R_D (c.c.)	$\mu_{app.}$ (D)
Benzene	−5·95	−0·692	$28{\cdot}6_2$	25·9	$0{\cdot}3_6$
Chlorobenzene	1·20	−0·325	61·9	31·7	$1{\cdot}2_2$
Nitrobenzene	31·6	−0·197	229·8	32·4	$3{\cdot}1_1$
Naphthalene	−4·31	−0·419	$43{\cdot}3_5$	44·3	*ca.* 0
Phenanthrene	−3·44	−0·295	$58{\cdot}9_4$	63·5	*ca.* 0
Carbon disulphide	−3·19	−0·207	$23{\cdot}5_1$	21·3	$0{\cdot}3_2$
Carbon tetrachloride	−2·85	0·067	$34{\cdot}1_2$	26·6	$0{\cdot}6_1$

TABLE 3. *Molar Kerr constants and sums of anisotropy and dipole terms at infinite dilution calculated from Tables* 1 *and* 2.

Solute	γ	δ	$_\infty(_mK_2) \times 10^{12}$	$(\theta_1 + \theta_2) \times 10^{25}$
Benzene	0·055	−2·95	$-5{\cdot}2_4$	$-1{\cdot}2_5$
Chlorobenzene	0·086	−6·98	101·5	$24{\cdot}1_4$
Nitrobenzene	0·094	−32·7	743·9	176·9
Naphthalene	0·173	−5·24	51·4	12·2
Phenanthrene	0·241	−4·77	71·0	16·9
Carbon disulphide	0·124	−3·54	17·0	$4{\cdot}0_4$
Carbon tetrachloride	0·008	−1·46	$-7{\cdot}0_3$	$-1{\cdot}6_8$

Turning now to the five normally non-polar solutes in Tables 2 and 3, we must conclude that in chloroform they exhibit θ_2 terms:

Solute	C_6H_6	$C_{10}H_8$	$C_{14}H_{10}$	CS_2	CCl_4
Apparent $\theta_2 \times 10^{35}$	−3·0	+0·8	−2·7	−2·6	−1·7

Such features point to the possession by these species of finite dipole moments, and are of interest in relation to previous [11-13] observations which had also suggested that non-polar solutes might become polar in polar media. The negative signs now noted for these values of θ_2 indicate that the apparent moments are developed in directions roughly perpendicular to the greatest polarisability axis of the dissolved particle, whatever this is—it might be some sort of loose adduct of chloroform with either a distorted or an undistorted form of the non-polar solute. On the probably over-simple assumption that benzene and carbon disulphide (semi-axes $\times 10^{23}$: 1·12, 1·12, $0{\cdot}73_5$ and 1·308, 0·558, 0·558 respectively [2]) are undistorted and behave independently of the chloroform molecules, dipole moments of 0·3—0·4 D would, if acting parallel to the b_3 directions, produce *negative* θ_2's about one-third to one-half of those found. With carbon tetrachloride (for which θ_1 is zero [14]) some distortion must be presumed. If μ_{C-Cl} is taken as *ca.* 1·6 D, then an apparent moment for carbon tetrachloride of 0·6 D implies modification of the tetrahedral model so that three of the Cl–C–Cl angles become 102°; with the values $b_L^{C-Cl} = 0{\cdot}399 \times 10^{-23}$ and $b_T^{C-Cl} = 0{\cdot}185 \times 10^{-23}$, the semi-axes for the distorted molecule would be $0{\cdot}982 \times 10^{-23}$ (along the line of action of $\mu_{resultant}$) and $1{\cdot}049 \times 10^{-23}$ (in the two directions perpendicular to $\mu_{resultant}$). These are to be compared with $b_1 = b_2 = b_3 = 1{\cdot}02_6 \times 10^{-23}$ ordinarily determined. The difference, $b_1 - b_2 = -0{\cdot}067 \times 10^{-23}$, combined with a moment of 0·6 D, leads to a θ_2 term of $-0{\cdot}63 \times 10^{-35}$, namely, about one-third of that actually recorded. It seems therefore that either the negativity of our θ_2 values has been overestimated or the apparent moments deduced are too small. The use of chloroform as a solvent in the measurement both of electric double refraction and of dielectric polarisation involves practical difficulties which are not present with the usual non-polar media, although, even in these, moments estimated from orientation polarisations of a few c.c. are notoriously uncertain (ref. 8, p. 25). We suspect the values of $\mu_{apparent}$ more than those of θ_2; to accept the former as real and to attempt the extraction of polarisability semi-axes in the usual way is dangerous because $45k^2T^2\theta_2/\mu^2_{apparent}$ is sensitively affected by $\mu^2_{apparent}$, small errors in which are much magnified in the quotient, *i.e.*, in the quantity $2b_1 - b_2 - b_3$.

With chloro- and nitro-benzene, however, the situation is better: using the apparent moments and θ_2's in Tables 2 and 3, we find semi-axes which are close to those previously noted [10] in carbon tetrachloride:

		$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$
C_6H_5Cl	in $CHCl_3$	1·53	1·21	0·84
	in CCl_4	1·48	1·26	0·82
$C_6H_5{\cdot}NO_2$	in $CHCl_3$	1·67	1·06	0·93
	in CCl_4	1·62	1·20	0·86

Apparent Moments of Chloro- and Nitro-benzene in Chloroform.—Values (in D) have been previously reported as: $\mu_{PhCl} = 1{\cdot}18$; [12] $\mu_{PhNO_2} = 3{\cdot}30$,[15] 3·24,[16] 3·17,[17] 3·05,[12] 3·15.[18] Although the μ's ($1{\cdot}2_2$ and $3{\cdot}1_1$ D) given in Table 2 for chloro- and nitro-benzene are reconcilable with most of these earlier data, it is nevertheless our experience that the determination of $\mu_{apparent}$ in chloroform is a less reliable procedure generally than when benzene, carbon tetrachloride, etc., are taken as solvents: the cases of naphthalene and

[11] Le Fèvre and Le Fèvre, *J.*, 1936, 487.
[12] Le Fèvre and Russell, *J.*, 1936, 491.
[13] Holland and Le Fèvre, *J.*, 1950, 2166.
[14] Le Fèvre, Le Fèvre, and Rao, *J.*, 1956, 708; Le Fèvre and Le Fèvre, *J.*, 1959, 2670.
[15] Hassel and Uhl, *Z. phys. Chem.*, 1930, *B*, **8**, 199.
[16] Hassel and Naeshagen, *Naturwiss.*, 1930, **18**, 24.
[17] Jenkins, *Nature*, 1934, **133**, 106; *J.*, 1934, 482.
[18] Smith and Cleverdon, *Trans. Faraday Soc.*, 1949, **45**, 109.

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phenanthrene, where R_0's calculated from the observed n_{12}'s and d_{12}'s inexplicably exceed the $_\infty P_2$'s, illustrate one of the uncertainties. This has relevance to the point of the last paragraph. If, *e.g.*, with nitrobenzene, a small change be imagined in $\mu_{apparent}$, recomputation will reveal that a notable alteration follows of the principal polarisabilities, especially of b_2 and b_3:

μ (D)	$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$
$3{\cdot}1_1$	1·67	1·06	0·93
$3{\cdot}2_1$	1·64	1·16	0·86
$3{\cdot}3_1$	1·62	1·22	0·83

Conclusion.—These results suggest that chloroform can be used as solvent for this work only with strongly polar solutes whose apparent moments in chloroform can be measured accurately.

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326. *Kinetic Measurements of the Acetylation of Anisole by Acetic Acid in the Presence of Boron Trifluoride.*

By V. GOLD and T. RILEY.

In the presence of large concentrations of boron trifluoride in acetic acid, anisole is converted into 4-methoxyacetophenone. The reaction velocity is very dependent on catalyst concentration, and it is tentatively suggested that acetylation is due to the acetyl cations formed in the equilibrium, $[AcOH_2]^+[BF_3{\cdot}OAc]^- \rightleftharpoons Ac^+ + BF_3{\cdot}OH^- + AcOH$.

THE aralkylation of anisole catalysed by sulphuric acid,[1,2] zinc chloride,[3] or boron trifluoride [4] in acetic acid solution can be conveniently observed without interference by disturbing side-reactions. During kinetic studies of these reactions it was found that, in the absence of an aralkylating agent, the interaction of acetic acid and anisole is slow and comparatively unimportant at catalyst concentrations in the range used in the aralkylation experiments. However, when much higher concentrations of boron trifluoride were used, anisole was acetylated at a conveniently measurable velocity, and these kinetic results are now reported. The reaction results in the introduction of one acetyl group, in qualitative agreement with earlier preparative work [5] under more drastic conditions.

EXPERIMENTAL

The preparation and analysis of catalyst solutions [4] and the purification of anisole [2] (samples of which were stored in the dark over sodium [6]) have been described previously.

4-Methoxyacetophenone was prepared (i) by Noller and Adams's procedure [7] (acetylation with acetic anhydride and aluminium trichloride in carbon disulphide; yield 68%; m. p. 38·5°), (ii) by a method involving conditions similar to those of the kinetic runs, and (iii) by the use of zinc chloride, hydrogen chloride, and acetic anhydride in acetic acid. In procedure (ii) anisole (3·2 g.) was added to a solution of boron trifluoride–acetic acid complex (40 ml.

[1] Bethell and Gold, *J.*, 1958, 1905.
[2] Bethell, Gold, and Riley, *J.*, 1959, 3134.
[3] Bethell and Gold, *J.*, 1958, 1930.
[4] Gold and Riley, *J.*, 1960, 2973.
[5] Kastner in "Newer Methods of Preparative Organic Chemistry," Interscience Publ. Inc., New York and London, 1948, p. 281; Oelschläger, *Arch. Pharm.*, 1955, **288**, 102.
[6] Bien, Kraus, and Fuoss, *J. Amer. Chem. Soc.*, 1934, **56**, 1860.
[7] Noller and Adams, *J. Amer. Chem. Soc.*, 1924, **46**, 1889.

containing *ca.* 19 g. of the trifluoride) in acetic acid (40 ml.). After being kept at 40° for 15 days, the solution was poured into ice-water. Ether-extraction, neutralisation, drying ($MgSO_4$) of the ether extract, and distillation under reduced pressure gave *ca.* 98% yield of 4-methoxyacetophenone, b. p. 143—144°/18 mm., identical with the specimen obtained by method (i). A vapour-phase chromatogram gave evidence of a single product only, indicating the absence of *ortho*- and *meta*-isomers. In method (iii) anisole (8 g.) and solutions of zinc chloride in acetic acid (53 ml. containing *ca.* 17 g. of zinc chloride) and of hydrogen chloride (*ca.* 3 g.) in acetic acid (50 ml.) were mixed and allowed to react at room temperature for 7 days. 4-Methoxyacetophenone indistinguishable from previous samples was isolated as before. The yield (4 g.) was 50%, based on the amount of acetic anhydride, but this figure is of doubtful significance in view of the possibility of acetylation by acetic acid. Method (i) was also used in the preparation of 2,4-dimethoxyacetophenone (80% yield) from *m*-dimethoxybenzene.

In kinetic experiments the reaction was initiated by addition of a measured amount of anisole to the catalyst solution at 40°. Samples of the mixture were quenched at timed intervals by running them into "AnalaR" ethanol and, after appropriate accurate dilution, analysed by spectrophotometry (Beckman DU instrument). Relevant blank measurements were performed and a small correction was applied for absorption due to the catalyst addition. The quenching of samples in ethanol (instead of acetic acid) was essential both in the present study and in that of the diphenylmethylation of anisole,[4] because the absorption spectra of anisole and boron trifluoride are not additive in acetic acid solution, whereas they are additive in ethanol solution. The non-additivity in acetic acid solution must be due to some interaction between the solutes which does not appear to be sufficiently extensive or profound (at least at lower concentrations of boron trifluoride) to affect the reactivity of anisole towards diphenylmethylation. It is possible that the ethanol–boron trifluoride interaction is stronger, so that any complex formation between anisole and boron trifluoride is effectively reversed on dilution of the sample in ethanol.

The reactions were of first order with respect to anisole, the acetylating agent (solvent) being in large excess. Rate constants are summarised in the Table.

First-order rate constants for acetylation of anisole by acetic acid at 40°.

(a) *Effect of catalyst concentration.* $[Anisole]_0 = 0{\cdot}192$M.

$[BF_3]$ (M)	4·98	5·26	5·88	6·12	6·46	6·74	7·05
10^6k_1 (sec.$^{-1}$)	3·75	4·94	10·9	13·5	23·0	28·7	39·2

(b) *Dependence on initial concentration of anisole.* $[BF_3] = 6{\cdot}74$M.

$10^3[Anisole]_0$ (M)	3·82	9·63	19·2
10^6k_1 (sec.$^{-1}$)	34·5	29·6	28·7

(c) *Effect of added water.* $[BF_3] = 6{\cdot}74$M. $[Anisole]_0 = 0{\cdot}0963$M.

$[H_2O]$ (M)	0	0·11	0·44
10^6k_1 (sec.$^{-1}$)	29·6	25·0	22·8

The progress of the reactions was attended by slow generation of an intense orange colour (due to the conjugate acid of the product) which was immediately discharged when a sample was quenched in ethanol. Quenched samples corresponding to long reaction times had an appreciable fluorescence. In some similar reactions such fluorescence has been attributed to the formation of pyrylium ions.[8] In view of the known conversion of acetophenone into pyrylium compounds in the presence of boron trifluoride,[9] this explanation appears very plausible in our reaction. At high acidities acetylation was complete before the fluorescence became noticeable, but at low acidities this subsequent reaction of the product interfered before completion of the acetylation, and infinity values of the optical densities had to be taken from the results for the faster reactions.

Discussion

The discussion of the mechanism of acetylation by boron trifluoride in acetic acid is intimately connected with the chemical equilibria in this system. In earlier work [4] it

[8] Burton and Praill, *J.*, 1951, 726; Lombard and Stéphan, *Compt. rend.*, 1953, **237**, 333.
[9] Dovey and Robinson, *J.*, 1935, 1389.

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was shown that the solutions produced have a marked power to promote ionisation in the sense

$$ROAc + (H^+) \longrightarrow R^+ + AcOH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

but it was not necessary—in that context—to consider the processes which led to the high level of acidity and low activity of acetic acid whose combined effect gives rise to the favourable equilibrium concentration of R^+ cations. In view of the general existence of complexes $BF_3,2AcOH$, boron trifluoride in acetic acid solution is plausibly considered [10] to be mainly in the form $[AcOH_2]^+[BF_3{\cdot}OAc]^-$. On this basis we can understand the observation [11] that solutions of boron trifluoride and of sulphuric acid in acetic acid have almost the same high acidity (since they both contain the same Brønsted acid species $AcOH_2^+$) and that boron trifluoride should be slightly superior to sulphuric acid in the promotion of equilibrium (1) by virtue of the formation of the ion $[BF_3{\cdot}OAc]^-$.[4]

There is evidence that the acetic acidium ion $AcOH_2^+$ is not a strong acetylating agent.[12] However, it is not certain that this evidence would exclude the possibility that high concentrations of the ion—such as are probably formed in the solutions of the present study—might be effective. Nevertheless, it seems unlikely that $AcOH_2^+$ is the species concerned in the attack on anisole for, if it were, one would expect the reaction rate to be proportional to the concentration of boron trifluoride. In fact, the reaction velocity shows a steeper dependence on catalyst concentration [see section (a) of the Table], and this points to the formation of an active acetylating species—most plausibly the acetyl cation $CH_3{\cdot}CO^+$—by a more complicated pre-equilibrium. (As the reaction is of first order with respect to anisole, the production of the acetylating agent cannot be rate-controlling.)

The formation of the acetyl cation from the conjugate acid of acetic acid is a dehydration which would be thermodynamically favoured by a low activity of water in the medium. It may be that this activity is particularly low in the boron trifluoride–acetic acid solutions because of an equilibrium $[BF_3{\cdot}OAc]^- + H_2O \rightleftharpoons [BF_3{\cdot}OH]^- + AcOH$ which tends to lie largely over to the right-hand side and thus effectively removes water from the medium. On the basis of this hypothesis the formation of acetyl cations would be represented by the reaction $[AcOH_2]^+[BF_3{\cdot}OAc]^- \longrightarrow [Ac]^+[BF_3{\cdot}OH]^- + AcOH$.

An explanation along these (or similar) lines finds support in the small effect of added water on the reaction velocity [section (c) of Table] and also in our earlier observation [4] that the ionisation of diarylmethyl acetate indicators in boron trifluoride–acetic acid solutions is only slightly changed when some of the acetic acid in the solvent is replaced by water, a result which seems to imply that the added water does not cause the replacement of acetic acidium ions by hydroxonium ions, but is removed by a process which has little effect on the acidity of the medium.[13]

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[*Received, October 24th*, 1960.]

[10] Greenwood and Martin, *Quart. Rev.*, 1954, **8**, 1.
[11] Meerwein, *Annalen*, 1927, **455**, 227.
[12] *E.g.*, Burton and Praill, *J.*, 1950, 1203.
[13] Cf. Wichterle, Laita, and Pazlar, *Chem. Listy*, 1955, **49**, 1612.

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327. *Trialkylplumbanes. Part I. Properties of the Trimethylplumbane–Borine–Ammonia System.*

By R. Duffy and A. K. Holliday.

Potassium borohydride and trimethylchloroplumbane react in liquid ammonia to give trimethyl-lead borohydride ammoniate, which on distillation gives ammonia–borine, ammonia, and trimethylplumbane; the latter reacts with the ammonia to form unstable green ammonium trimethylplumbate, but the plumbane is not recovered by addition of diborane or boron trifluoride. Ammonium trimethylplumbate decomposes first to the red pentamethyldiplumbate and finally to lead, tetramethylplumbane, hydrogen, and methane; it reacts with trimethylchloroplumbane in liquid ammonia to give hexamethyldiplumbane, but does not react with ethylene or diazomethane. Solutions of trimethylplumbane in trimethylamine are less stable than in ammonia.

In a preliminary communication [1] we reported the preparation of trimethylplumbane by reaction of trimethylchloroplumbane with potassium borohydride in liquid ammonia. Preparation by reduction of trimethylchloroplumbane with lithium aluminium hydride in dimethyl ether between −90° and −110° has since been reported, together with some properties of the plumbane.[2,3] The instability of the crude plumbane under our conditions of preparation prompted this investigation of the plumbane–ammonia–borine system; properties and reactions of the pure plumbane will be given in Part II.

Slow removal of solvent ammonia at −78° from an equimolar trimethylchloroplumbane–potassium borohydride mixture left potassium chloride and a white solid which decomposed slowly at 0° and more rapidly at 20° to given hydrogen, methane, ammonia, tetramethylplumbane, and a residue of lead and "ammonia–borine," $(H_3N,BH_2)_n$. In individual experiments the relative amounts of the products other than ammonia–borine varied, but the overall material balance was consistent and indicated an empirical formula $Me_3Pb(BH_4),xNH_3$ ($x < 2$) for the white solid. Decomposition in presence of excess of solvent gave the same products. The absence of trimethylborine or its ammonia adduct from these is notable, since decomposition of the very unstable volatile trimethyl-lead borohydride gave trimethylborine, lead, and hydrogen.[4] Hence co-ordination of ammonia to the borohydride converts the latter into a less volatile solid, increases its stability prevents the re-arrangement necessary to form boron–carbon bonds, and permits instead the ready formation of ammonia–borine; the observed characteristics of the latter were those expected for $(H_3N,BH_3)_n$ rather than for the "diammoniate of diborane," $[(H_3N)_2BH_2]BH_4$.[5] Removal of a borine group from the trimethyl-lead borohydride would give trimethylplumbane; there was therefore the possibility that "Me_3PbBH_4,xNH_3" was a mixture of ammonia–borine and an ammoniated trimethylplumbane (*e.g.*, $NH_3,PbHMe_3$). Careful distillation of the trimethyl-lead borohydride at −5° did yield the plumbane, ammonia, and ammonia–borine in the amounts expected, *i.e.*:

$$Me_3PbBH_4,xNH_3 \longrightarrow PbHMe_3 + (x-1)NH_3 + H_3N,BH_3$$

These products were separated by fractionation at −100°, giving the plumbane as a liquid. It was then found that mixtures of the plumbane and ammonia were much less stable than either the plumbane alone or the trimethyl-lead borohydride ammoniate. Hence presence of ammoniated plumbane in the latter is unlikely, and decomposition proceeds as given in the equation above.

[1] Duffy and Holliday, *Proc. Chem. Soc.*, 1959, 124.
[2] Amberger, *Angew. Chem.*, 1960, **72**, 494.
[3] Becker and Cook, *J. Amer. Chem. Soc.*, 1960, **82**, 6264.
[4] Holliday and Jeffers, *J. Inorg. Nuclear Chem.*, 1958, **6**, 134.
[5] Shore and Parry, *J. Amer. Chem. Soc.*, 1958, **80**, 8.

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Some information as to the nature of the ammonia–plumbane interaction was obtained from the proton magnetic resonance spectrum of the mixture. A detailed examination of the spectrum of the pure plumbane will be reported in Part II; it is sufficient to note here that two main absorption bands were found, the larger due to the hydrogen atoms of the three methyl groups and the smaller, on the low-field side, to the single hydride-hydrogen atom. Addition of ammonia to the plumbane shifted the latter band nearer to the larger band, suggesting increased shielding of the hydride hydrogen, and this indicated a rapid exchange with the hydrogen atoms of the added ammonia, which could clearly be due to ammoniation: $NH_3 + Me_3PbH \longrightarrow NH_4(PbMe_3)$.

When an equimolar mixture of the plumbane and ammonia was kept at −78°, the originally colourless liquid rapidly became green; loss of 0·5 mol. of methane followed, to give a bright red solid, stable at this temperature. Warming to −45° then gave hydrogen, methane, ammonia, tetramethylplumbane, hexamethyldiplumbane, and lead; the diplumbane, on further warming, gave more tetramethylplumbane and lead, and the overall balance corresponded to Pb_2HMe_5,NH_3. If ammonia was first removed from the red solid at −78°, slow decomposition followed giving finally methane, tetramethylplumbane, and lead, in amounts corresponding to decomposition of Pb_2HMe_5. Trimethylplumbane dissolved in an excess of liquid ammonia at −78°; a green solution was formed immediately, slowly changing to red with evolution of methane and then decomposing further to give more methane, lead, and tetramethylplumbane ($Pb : PbMe_4 = 1 : 1$). These results can be accounted for by the reactions (1—5):

$$Me_3PbH + NH_3 \longrightarrow NH_4[PbMe_3]\ (\text{green}) \quad (1)$$

$$NH_4[PbMe_3] \longrightarrow PbMe_3 + MeH + NH_3 \quad (2)$$

$$NH_4[PbMe_3] + PbMe_3 \longrightarrow NH_4[Pb_2Me_5]\ (\text{red}) \quad (3)$$

$$NH_4[Pb_2Me_5] \longrightarrow Pb + PbMe_4 + MeH + NH_3 \quad (4)$$

or

$$2NH_4[Pb_2Me_5] \longrightarrow Pb + PbMe_4 + Pb_2Me_6 + 2NH_3 + H_2 \quad (5)$$

The alternative elimination of methane from the $[PbMe_3]^-$ anion by ammonolysis to give, *e.g.*, $[PbMe_2NH_2]^-$, postulated for solutions of potassium trimethylplumbate in ammonia,[6] seems improbable in presence of ammonium ion. Although polylead anions are known (*e.g.*, Pb_9^{4-}), alkylplumbanes containing more than two lead atoms have not been reported, and further linking of $PbMe_2$ groups to $[Pb_2Me_5]^-$ ions also seems unlikely.

Attempts to remove ammonia from plumbane–ammonia mixtures by addition of acceptors such as diborane or boron trifluoride did not give appreciable amounts of plumbane, probably because the heat of the ammonia–borine reaction produced too rapid a decomposition of remaining ammonium trimethylplumbate. The plumbane–ammonia mixture did not react with diazomethane, ethylene, or methyl chloride; reaction with at least one of these might have been expected, since the hydride-hydrogen atom of the plumbane must be fairly labile; the absence of reaction is further evidence of the formation of an ammonium salt. This is again supported by the reaction of trimethylchloroplumbane with a solution of trimethylplumbane in liquid ammonia at −78°; the green colour disappeared immediately, but only a trace of methane was formed, the products being hexamethyldiplumbane (appearing finally as lead and tetramethylplumbane) and ammonium chloride in 90% yield: $NH_4[PbMe_3] + Me_3PbCl \longrightarrow Pb_2Me_6 + NH_4Cl$.

A solution of pure trimethylplumbane (free from ammonia) in an excess of trimethylamine decomposed much more rapidly than in ammonia, and only a faint transient red colour was observed before the solution blackened owing to deposition of lead; no break in methane evolution at the stage $MeH : Me_3PbH = 0{\cdot}5 : 1$ was detected and the final ratios were $MeH : Pb : Me_4Pb = 1 : 1 : 1$. Formation of trimethylammonium trimethylplumbate would be easier than that of the ammonium salt, but the subsequent decomposition reactions (2)—(5) would not be expected to occur more readily. In reaction (3) the trimethylplumbate ion is acting as donor to the dimethyl-lead molecule in preference to

[6] Holliday and Pass, *J.*, 1958, 3485.

ammonia; with trimethylamine, the alternative reaction $Me_3N + PbMe_2 \longrightarrow Me_3N,PbMe_2$ may predominate, preventing formation of much red pentamethyldiplumbate and causing rapid disproportionation of the dimethyl-lead.

Trimethylstannane has been prepared by the reaction [7]

$$Me_3SnNa + NH_4Cl \xrightarrow{NH_3} SnHMe_3 + NaCl + NH_3$$

and trimethylgermane similarly.[8] This type of reaction does not yield trialkylplumbanes, giving, instead, alkanes, lead halides, and R_3Pb compounds.[9] It is now clear that the failure of this method is not due primarily to the instability of the trialkylplumbane, but to the polarity of the molecule in the sense Me_3Pb^-–H^+, which makes proton abstraction by solvent ammonia easy but forms a salt less stable than the plumbane itself.

Experimental

Starting Materials.—Ammonia from a cylinder was dried with sodium and stored as gas after fractionation in a high-vacuum system; all other volatile materials were similarly fractionated until correct vapour pressures and infrared spectra were obtained. Potassium borohydride was extracted with liquid ammonia and the extract crystallised. Trimethylchloroplumbane was prepared by reaction of dry hydrogen chloride with tetramethylplumbane in hexane.[10]

All experiments were conducted with a high-vacuum apparatus, and reaction tubes were only opened to atmosphere for treatment of involatile residues. Tetramethylplumbane was estimated by weight after condensation in a weigh-bulb at −196°, lead by precipitation as chromate, and boron as boric acid by titration in presence of mannitol.

Potassium Borohydride–Trimethylchloroplumbane Reactions (Units are mmoles unless otherwise stated).—Reaction times and temperatures varied between 3 min. at −75° to 191 hr. at −33°. In a typical experiment, potassium borohydride (0·99) was added to trimethylchloroplumbane (0·99) in about 9 ml. of liquid ammonia at −33°; shaking gave a white precipitate, with no further change after 191 hr. at −33°, and no non-condensable gas. After slow removal of solvent at −78° the white solid left decomposed slowly at 0° and steadily at 20°, giving after 24 hr. methane (0·15), hydrogen (0·36), tetramethylplumbane (0·66), and ammonia (1·26) as volatile products. A further 24 hr. at 20° gave hydrogen (0·04) only. Water (5 ml.) was condensed into the tube at −196°; hydrolysis at 100° for 20 hr. then gave hydrogen (2·72), ammonia (0·83), and boric acid (0·92), with lead (0·26) in the residue. Hence recovery ratios relative to Pb = 1·00 were $CH_3 : H : NH_3 = 3·01 : 1·04 : 1·37$ before hydrolysis and $H : B : NH_3 = 2·96 : 1·00 : 0·90$ after hydrolysis; overall H = 4·00. No loss of potassium or chloride ion occurred from the residue.

Separation of trimethylplumbane–ammonia and its decomposition. After initial reaction between trimethylchloroplumbane (0·99) and potassium borohydride (0·98), solvent was removed and the white product held at −5°; material volatile at this temperature was distilled off it through a short path and condensed as a white solid at −196°. The latter, when kept at −78°, produced a green solution which slowly changed to a red solid stable at this temperature, with evolution of methane (0·39). Allowing the temperature to rise slowly caused the red solid to darken and decompose with effervescence at −45°. After 6 hr. at 20° the volatile products were methane (0·14), hydrogen (0·12), ammonia (0·75), and tetramethylplumbane (0·26). The residue contained lead and off-white crystals, m. p. 36° (hexamethyldiplumbane has m. p. 38°). Decomposition of the latter was complete at 95°, giving tetramethylplumbane (0·22), and hydrogen (0·07) also appeared here. Hydrolysis of the residue at 100° gave hydrogen (0·12), boric acid (0·07), ammonia (0·05), and lead (0·32). If hydrogen recovered at 95° and by hydrolysis is presumed to come from ammonia–borine (0·07) present as impurity (requiring H, 0·21; found, 0·19), recovery ratios relative to Pb = 1·00 are: overall, $Me : H : NH_3 = 3·06 : 0·96 : 0·94$; red solid, $Me : H : NH_3 = 2·57 : 0·48 : 0·94$.

Decomposition of Trimethylplumbane in an Excess of Liquid Ammonia.—Trimethylplumbane

[7] Kraus and Greer, *J. Amer. Chem. Soc.*, 1922, **44**, 2629.
[8] Kraus and Flood, *J. Amer. Chem. Soc.*, 1932, **54**, 1635.
[9] Gilman and Bailie, *J. Amer. Chem. Soc.*, 1939, **61**, 731.
[10] Calingaert, Dykstra, and Shapiro, *J. Amer. Chem. Soc.*, 1945, **67**, 190.

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(0·71) was condensed at −196° on to ammonia (*ca.* 500) also at −196°. A pale green solution was formed as the solvent melted at −78°; at this temperature the colour gradually darkened and methane was evolved. After 17 hr. a red solution had been formed and the rate of methane evolution then decreased rapidly; slow evolution continued as the solution again became green, then colourless, lead being deposited. Until the solution became colourless, cooling to −196° to remove methane produced an orange-red solid. Methane evolution ceased (total 0·73) after 190 hr. at −78°, with no more produced at −33°. In another experiment, the reaction was accelerated by warming to −33° and all the methane was evolved; solvent was then removed and tested to ensure that no tetramethylplumbane had been distilled off. Storage at 20° for 14 hr. then gave tetramethylplumbane (0·18), ammonia (0·01), and non-condensable gas (0·01), with some hexamethyldiplumbane; the diplumbane decomposed at 95°, to give more tetramethylplumbane (0·17), and hydrogen (0·09) was also recovered from ammonia–borine as impurity. The black residue gave on hydrolysis lead (0·36), hydrogen (0·13), boric acid (0·08), and ammonia (0·06). After allowance for ammonia–borine as before, with total Pb = 1·00, ratios were Pb : $PbMe_4$: CH_4 = 0·51 : 0·50 : 1·03, total Me = 3·02.

Decomposition of Trimethylplumbane in an Excess of Trimethylamine.—The reaction was treated as for the reaction with excess of ammonia (see above); trimethylplumbane (1·17) was added and melting at −78° gave a green solution which immediately blackened with only transient red coloration; methane (0·96) was produced after 3 min., finally 1·14 mol. after 28 hr., the solution then being colourless and lead having been deposited. Solvent was removed as before, leaving tetramethylplumbane (0·29) and hexamethyldiplumbane which gave more tetramethylplumbane (0·31); the amount of lead was 0·57 mol. Hence total Pb being taken as 1·00, ratios were Pb : $PbMe_4$: CH_4 = 0·49 : 0·51 : 0·97, total Me = 3·01.

Removal of Ammonia from Ammonium Pentamethyldiplumbate.—The diplumbate (0·44) was prepared as described above and held at −78° while ammonia was distilled from it in a closed system to a tube held at −196°. The red material began to blacken and non-condensable gas was formed. When no more ammonia could be extracted (172 hr.), evolution of non-condensable gas (methane 0·27; hydrogen 0·07) also ceased; ammonia was removed (1·71). The residue contained tetramethylplumbane (0·48), and the involatile part finally gave more tetramethylplumbane (0·02), lead (0·37), and ammonia–borine (0·10). With Pb = 1·00, ratios from the decomposition were CH_3 : hydride H = 2·56 : 0·47; methane evolved in initial formation of the diplumbate was 0·49 mol.

Ammonium Trimethylplumbate–Trimethylchloroplumbane Reaction.—To a mixture of trimethylplumbane (1·08) and ammonia (~500) trimethylchloroplumbane (1·23) was added at −78°; the green colour was immediately discharged and a white precipitate formed; only little methane (0·07) was present and no more was formed at −33°. After removal of solvent, partial melting of the residue occurred at 37°, indicating presence of hexamethyldiplumbane; the latter was decomposed to tetramethylplumbane (1·62) and lead (0·52). The hydrolysate yielded ammonium chloride (1·02) and trimethylchloroplumbane (0·17).

In an experiment where trimethylplumbane and ammonia were produced as above, pumping at 10^{-4} mm. gave sufficient transfer of a white solid which sublimed slowly and gave on hydrolysis boron (boric acid) (0·68), hydrogen (2·09 milliequiv.), and ammonia (0·65).

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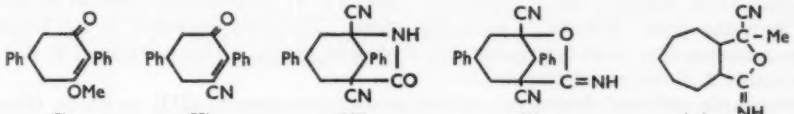
328. *Cyclohexane-1,3-diones. Part V.*[1] *Reaction of 3-Methoxy-2,5-diphenylcyclohex-2-en-1-one with Acetone Cyanohydrin.*

By B. E. Betts and W. Davey.

The reaction of 3-methoxy-2,5-diphenylcyclohex-2-en-1-one with acetone cyanohydrin to give 3-cyano-2,5-diphenylcyclohex-2-en-1-one has been reinvestigated and the structure of an additional product, 1,5-dicyano-3,8-diphenyl-6-azabicyclo(3,2,1)octan-7-one has been elucidated. Dehydrogenation of both products to *p*-terphenyl derivatives is described.

Nazarov, Akhrem, and Kamernitsky [2] showed that cyanohydrins can be prepared conveniently by the base-catalysed reaction of the parent ketone with acetone cyanohydrin, and also [3] that β-cyano-ketones are obtained from unsaturated ketones. In Part II [4] it was shown that the product thus obtained from 3-methoxy-2,5-diphenylcyclohex-2-en-1-one (I) was the 3-cyano-compound (II). This reaction and its products have now been investigated further.



Conditions for the formation of the cyano-ketone (II) were critical. The optimum conditions, which gave yields of 60—70%, were achieved by slightly basifying a solution of the enol ether (I) in purified acetone cyanohydrin with methanolic potassium hydroxide or triethylamine and storing the mixture overnight. No reaction occurred in non-basic media, and, when excess of potassium hydroxide was used, it was difficult to isolate the cyano-ketone (II). It was desirable to remove free acid from commercial acetone cyanohydrin by distillation. From reaction on a 150-g. scale, triethylamine being used as catalyst, there was obtained a 67% yield of the cyano-ketone (II) together with 4% of a by-product, $C_{21}H_{17}ON_3$. The latter was the sole product (27% yield) of reaction at 80—90°.

To determine whether the cyano-ketone (II) was formed only in acetone cyanohydrin, the enol ether (I) was treated with aqueous-ethanolic potassium cyanide. No reaction occurred, but when acetic acid was added the enol ether (I) was hydrolysed to 2,5-diphenylcyclohexane-1,3-dione. All attempts to convert 3-chloro-2,5-diphenylcyclohex-2-en-1-one into the cyano-ketone (II) by exchange with acetone cyanohydrin or by addition to aqueous ethanolic potassium cyanide gave unchanged material. When 3-chloro-2,5-diphenylcyclohex-2-en-1-one was refluxed with sodium cyanide in dimethylformamide an 80% yield of 2′-hydroxy-*p*-terphenyl was obtained.

The formula $C_{21}H_{17}ON_3$ suggested addition of two molecules of hydrogen cyanide to the initial exchange product (II); but the molecular weight (by Rast's method) was 184 compared with a required value of 327. The same compound was formed from the cyano-ketone (II) and acetone cyanohydrin at 90°, suggesting that the latter was an intermediate in the formation of the new compound. Structure 1,3,3-tricyano-2,5-diphenylcyclohexanol was not supported by the infrared spectrum, which pointed strongly [5a] to the

[1] Part IV, *J.*, 1958, 1784.
[2] Nazarov, Akhrem, and Kamernitsky, *J. Gen. Chem., U.S.S.R.*, 1954, **25**, 1291 (U.S. translation).
[3] Nazarov and Zavyalov, *J. Gen. Chem. U.S.S.R.*, 1954, **24**, 475 (U.S. translation).
[4] Part II, Ames and Davey, *J.*, 1957, 3480.
[5] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1958, (*a*) pp. 205, 249, and 269, (*b*) p. 220, (*c*) p. 139.

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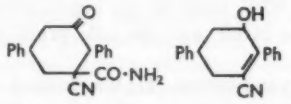
structure (III) as against the possible alternative (IV).* Compound (III) could result from intramolecular rearrangement of an intermediate cyanohydrin as occurs in the formation of 2,2,5,5-tetramethyloxazolid-4-one [7] from acetone and acetone cyanohydrin. The absorption band at 1220 cm.$^{-1}$ would then be due to a C–N or mixed OCN and NH vibration [5b] rather than a C–O vibration.

The suspected azabicyclo-octanone (III) was reconverted into the cyano-ketone (II) by hydrochloric–acetic acid or pyridine. 2′-Hydroxy-*p*-terphenyl was formed when the azabicyclo-octanone (III) was heated above its melting point. Since this was the sole product from similarly heating the cyano-ketone (II), the decomposition of the azabicyclo-octanone (III) may have proceeded *via* the cyano-ketone (II). Clearly the carbon skeleton of the cyano-ketone (II) is retained in the compound $C_{21}H_{17}ON_3$. Furthermore, the low value for the molecular weight of the azabicyclo-octanone (III) may be due to this ready thermal decomposition.

Further evidence for the formation of the azabicyclo-octanone (III) was provided by the isolation of the corresponding *N*-acetyl-, *N*-benzoyl-, and *N*-3,5-dinitrobenzoyl-derivatives. Dehydrogenation of the *N*-acetyl derivative afforded a compound $C_{20}H_{12}N_2$ having an ultraviolet spectrum typical of a terphenyl system.[4] Absorption bands corresponding to an aromatic nitrile (2222 cm.$^{-1}$) and a C–H deformation mode of an isolated free hydrogen atom (899 cm.$^{-1}$) were also noted. No band appeared in the frequency range corresponding to two adjacent free hydrogen atoms. This compound is therefore presumably 2′,6′-dicyano-*p*-terphenyl.

No simple carbonyl derivatives of the azabicyclo-octanone (III) could be obtained. Treatment with hydroxylamine hydrochloride, semicarbazide hydrochloride, or phenylhydrazine furnished products believed to be mono-derivatives of 1-cyano-3-oxo-2,5-diphenylcyclohexane-1-carboxyamide (V), formed by hydrolysis of the azabicyclo-octanone (III) and simultaneous loss of hydrogen cyanide. Reaction of the azabicyclo-octanone (III) with sodium sesquicarbonate, as for the preparation of the oxime, yielded a mixture of three compounds, one of which is considered to be the expected amide (V). An attempt to correlate this material with the derived oxime was unsuccessful, for treatment with hydroxylamine yielded only an uncrystallisable oil.



(V) (VI)

The effect of stronger alkali was next investigated. Treatment of the azabicyclo-octanone (III) with one equiv. of sodium hydroxide gave a high yield of one of the compounds previously obtained by the action of sodium sesquicarbonate. When this experiment was repeated in the presence of excess of methyl iodide the sole product was the cyano-ketone (II). Finally, with excess of sodium hydroxide the azabicyclo-octanone (III) afforded 2′-hydroxy-*p*-terphenyl, as did the cyano-ketone (II), indicating that the decomposition of the azabicyclo-octanone (III) proceeded *via* the cyano-ketone (II).

Dehydrogenation of the cyano-ketone (II) and derived compounds was investigated as a means of determining the orientation of other isomeric cyano-ketones (cf. Part VII). As in Part II,[4] no recognisable product could be isolated after heating the cyano-ketone (II) with sulphur or selenium. Unchanged cyano-ketone (II) was recovered from attempted

* Ayres and Raphael [6] obtained a compound $C_{11}H_{16}ON_2$ from 1-acetylcyclohept-1-ene and aqueous ethanolic potassium cyanide which they considered to be 8-cyano-10-imino-8-methyl-9-oxabicyclo(5,3,0)decane (A).

[6] Ayres and Raphael, *J.*, 1958, 1779.

[7] Ultee, *Rec. Trav. chim.*, 1909, **28**, 259; Snyder and Elston, *J. Amer. Chem. Soc.*, 1954, **76**, 3039; see also Pinner, *Ber.*, 1884, **17**, 2009.

dehydrogenation with chloranil and also after treatment with *N*-bromosuccinimide. Dehydrogenation of the corresponding cyano-alcohol (VI) with sulphur had previously [4] been found to give only *p*-terphenyl (7%). 3-Cyano-2,5-diphenylcyclohex-2-en-1-ol (VI) and its acetate were recovered unchanged from treatment with chloranil or palladium–charcoal in boiling *p*-cymene.

The cyano-alcohol (VI) and *N*-bromosuccinimide gave 4-bromo- and 6-bromo-3-cyano-2,5-diphenylcyclohex-2-en-1-one. Both bromo-compounds were dehydrobrominated in pyridine to 2′-cyano-6′-hydroxy-*p*-terphenyl.

Experimental

Ultraviolet absorption spectra were determined in 96%ethanol, with a Unicam S.P. 500 Spectrophotometer. Figures in italics denote inflexions. " Light petroleum " refers to the fraction, b. p. 60—80°.

Reaction of 3-*Methoxy*-2,5-*diphenylcyclohex*-2-*en*-1-*one* (I) *with Acetone Cyanohydrin.*—(a) 3-*Cyano*-2,5-*diphenylcyclohex*-2-*en*-1-*one* (II). 3-Methoxy-2,5-diphenylcyclohex-2-en-1-one (1·0 g.) and redistilled acetone cyanohydrin (10 c.c.) containing 13% methanolic potassium hydroxide (0·2 c.c.) were set aside overnight and then poured into water and acidified (Congo Red). The product was crystallised from ethyl acetate–light petroleum, giving 3-cyano-2,5-diphenylcyclohex-2-en-1-one (0·7 g.), m. p. 155° (Found: C, 83·3; H, 5·6; N, 5·2. Calc. for $C_{19}H_{15}NO$: C, 83·5; H, 5·5; N, 5·1%). Ames and Davey [4] gave m. p. 148—149°; a mixture melted at 152—153°.

When heated above its m. p., the cyano-ketone decomposed quantitatively to 2′-hydroxy-*p*-terphenyl, m. p. and mixed m. p. 194°. The cyano-ketone formed an *oxime*, needles, m. p. 225° (from ethanol) (Found: C, 77·2; H, 6·2; N, 9·4. $C_{19}H_{16}N_2O,\frac{1}{2}H_2O$ requires C, 76·7; H, 5·8; N, 9·4%).

(b) 1,5-*Dicyano*-3,8-*diphenyl*-6-*azabicyclo*(3,2,1)*octan*-7-*one* (III). The enol ether (2·0 g.), purified acetone cyanohydrin (20 c.c.), and triethylamine (0·1 c.c.) were heated for 45 min. at 80—90°. The solution was poured into water, and the solid collected and dried. 1,5-*Dicyano*-3,8-*diphenyl*-6-*azabicyclo*(3,2,1)*octan*-7-*one* (0·6 g.) crystallised from ethyl acetate–light petroleum in prisms, m. p. 225° [Found: C, 76·7; H, 5·1; N, 12·9%; *M* (Rast), 184. $C_{21}H_{17}N_3O$ requires C, 77·0; H, 5·2; N, 12·8%; *M*, 327]; $\lambda_{max.}$ *235*, *257*, *263*, and 292 mμ (ε 3200, 1450, 1200, 1300 respectively); infrared spectrum (KBr disc), bands at 3257 (NH, fused ring γ-lactam), 2247 (C⋮N), 1715 (C=O, fused ring γ-lactam), 1600, 1585, 1493, 1449 (aromatic −C=C−), 1220 (C−N?), 766, 740, and 697 cm.$^{-1}$ (phenyl system).

Use of 3-cyano-2,5-diphenylcyclohex-2-en-1-one in place of the enol ether furnished the same azabicyclo-octanone (35%), m. p. and mixed m. p. 225°. When heated above its m. p. the azabicyclo-octanone decomposed quantitatively to 2′-hydroxy-*p*-terphenyl, m. p. and mixed m. p. 194°.

(c) The enol ether (155 g.) and purified acetone cyanohydrin (400 c.c.) containing triethylamine (3·0 c.c.) were set aside overnight. 3-Cyano-2,5-diphenylcyclohex-2-en-1-one (56 g.), m. p. and mixed m. p. 155°, was filtered off and the mother-liquor was poured into water. The solid material was collected, dried, and recrystallised from ethyl acetate, giving 1,5-dicyano-3,8-diphenyl-6-azabicyclo(3,2,1)octan-7-one (6·0 g.), m. p. and mixed m. p. 225°, followed by more cyano-ketone (46 g.), m. p. and mixed m. p. 155°.

6-*Acetyl*-1,5-*dicyano*-3,8-*diphenyl*-6-*azabicyclo*(3,2,1)*octan*-7-*one*.—The azabicyclo-octanone (0·8 g.) was refluxed for 1 hr. with acetic anhydride (8 c.c.) containing one drop of concentrated sulphuric acid. The mixture was poured into water (200 c.c.) and left overnight. The solid was recrystallised from ethyl acetate, giving the N-*acetyl derivative* (0·6 g.), needles, m. p. 272° (Found: C, 74·8; H, 5·3; N, 11·3. $C_{23}H_{19}N_3O_2$ requires C, 74·8; H, 5·2; N, 11·4%); $\lambda_{max.}$ 246, 251, 257, *263*, *269*, *292* mμ (ε 2900, 2900, 2800, 2350, 1700, 610 respectively); infrared spectrum (KBr disc), bands at 2247, 2237 (C⋮N), 1754, 1698 (CO−N−CO), and 1217 cm.$^{-1}$ (C−N?).

2′,6′-*Dicyano*-p-*terphenyl*.—The *N*-acetyl derivative (2·9 g.) was heated with selenium (3·0 g.) for 1 hr. at 300—350° and the residue was extracted with ethanol. Concentration of this extract afforded 2′,6′-*dicyano*-p-*terphenyl* (0·3 g.), needles, m. p. 236° (from ethyl acetate) (Found: C, 85·2; H, 4·4; N, 10·4. $C_{20}H_{12}N_2$ requires C, 85·7; H, 4·3; N, 10·0%); $\lambda_{max.}$ 210, 232, and 279 mμ (ε 40,700, 31,500, 22,200 respectively); infrared spectrum (KBr disc), bands

at 2222 (aromatic C⋮N), 1595, 1575, 1497, 1451 (aromatic −C=C−), and 899 cm.$^{-1}$ (C−H, isolated free hydrogen).

6-*Benzoyl*-1,5-*dicyano*-3,8-*diphenyl*-6-*azabicyclo*(3,2,1)*octan*-7-*one*.—The azabicyclo-octanone (0·5 g.) in dry pyridine (5 c.c.) was refluxed with benzoyl chloride (0·2 g.) for 2 hr. to give the *N-benzoyl derivative* (0·5 g.), prisms, m. p. 227° (from ethyl acetate) [Found: C, 78·0; H, 5·1; N, 9·7%; *M* (Rast), 324. $C_{28}H_{21}N_3O_2$ requires C, 77·9; H, 4·9; N, 9·7%; *M*, 431]; $\lambda_{max.}$ 244, *263*, 270, and 281 mμ (ε 15,350, 4000, 2450, 1650 respectively); infrared spectrum (KBr disc), bands at 2247, 2237 (C⋮N), 1745, 1684 (CO−N−CO), and 1255 cm.$^{-1}$ (C−N?).

The *N*-3,5-*dinitrobenzoyl derivative*, needles, m. p. 262° (from benzene) (Found: C, 64·6; H, 3·4; N, 13·2. $C_{28}H_{19}N_5O_6$ requires C, 64·5; H, 3·7; N, 13·4%), was similarly prepared.

Conversion of the Azabicyclo-octanone into 3-*Cyano*-2,5-*diphenylcyclohex*-2-*en*-1-*one*.—(a) *With pyridine*. The azabicyclo-octanone (1·0 g.) was refluxed in dry pyridine (10 c.c.) for 3 hr., and the solution then poured into dilute hydrochloric acid; the cyano-ketone (0·7 g.), m. p. and mixed m. p. 155°, was obtained.

(b) *In acid solution*. The azabicyclo-octanone (0·7 g.), acetic acid (10 c.c.), concentrated hydrochloric acid (7 c.c.), and water (4 c.c.) were refluxed for 12 hr., then diluted with water to give the cyano-ketone (0·6 g.), m. p. and mixed m. p. 155°.

Treatment of the azabicyclo-octanone (0·7 g.) with methylmagnesium iodide (from 0·1 g. of magnesium and 0·5 g. of methyl iodide) also yielded the cyano-ketone (0·4 g.), presumably owing to hydrolysis during the working up.

Reactions of 1,5-*Dicyano*-3,8-*diphenyl*-6-*azabicyclo*(3,2,1)*octan*-7-*one in Alkali*.—(a) *With sodium sesquicarbonate*. Sodium sesquicarbonate (1·5 g.) in water (30 c.c.) was refluxed with the azabicyclo-octanone (6·4 g.) in ethanol (450 c.c.) for 3 hr. The solvents were evaporated *in vacuo* and the residue was diluted with water. The solid was filtered off, dried, and successively extracted with ethyl acetate, methanol, and dimethylformamide. Evaporation of these extracts afforded, respectively, (i) 1-*cyano*-3-*oxo*-2,5-*diphenylcyclohexane*-1-*carboxyamide* (0·4 g.), needles, m. p. 218° (from ethyl acetate) [Found: C, 75·3; H, 5·5; N, 9·2%; *M* (Rast), 288. $C_{20}H_{18}N_2O_2$ requires C, 75·4; H, 5·7; N, 8·8%; *M*, 318], (ii) *compound A* (0·2 g.), prisms, m. p. 248° (from methanol) [Found: C, 75·4; H, 5·7; N, 8·7. $(C_{10}H_9NO)_n$ requires C, 75·4; H, 5·7; N, 8·8%], and (iii) *compound B* (2·5 g.), prisms, m. p. 334—335° (from dimethylformamide) [Found: C, 72·7; H, 5·5; N, 12·7. $(C_{21}H_{19}N_3O_2)_n$ requires C, 73·0; H, 5·5; N, 12·2%]. The molecular weights of these compounds could not be determined by Rast's method as they were insoluble in camphor. The infrared spectrum of 1-cyano-3-oxo-2,5-diphenylcyclohexane-1-carboxyamide showed bands (KBr disc) at 3370, 3310 (NH), 2247 (C⋮N), 1720 (C=O, cyclohexanone), 1690 (C=O, amide), 752, 700 cm.$^{-1}$ (phenyl system).

(b) *Carbonyl derivatives*. Treatment of the azabicyclo-octanone with hydroxylamine hydrochloride and sodium sesquicarbonate gave 1-*cyano*-3-*oxo*-2,5-*diphenylcyclohexane*-1-*carboxyamide oxime* as an amorphous powder, m. p. 208° (from ethyl acetate) (Found: C, 72·0; H, 6·0; N, 12·4. $C_{20}H_{19}N_3O_2$ requires C, 72·1; H, 5·7; N, 12·6%); infrared spectrum, bands (KBr disc) at 3450 (OH), 3333, 3190 (NH), 2250 (C⋮N), 1678, 1696 cm.$^{-1}$ (C=O, amide I and II).

Use of semicarbazide hydrochloride and sodium acetate likewise gave the corresponding *semicarbazone* as an amorphous powder, m. p. 198° (from benzene) (Found: C, 66·9; H, 5·8; N, 19·1. $C_{21}H_{21}N_5O_2$ requires C, 67·2; H, 5·6; N, 18·7%).

The azabicyclo-octanone (0·3 g.) in ethanol (15 c.c.) was refluxed with phenylhydrazine (0·1 g.) for 4 hr. to give the corresponding *phenylhydrazone* (30 mg.), orange prisms, m. p. 238—239° (from ethyl acetate–light petroleum) [Found: C, 76·3; H, 5·9; N, 14·2%; *M* (Rast), 272. $C_{26}H_{24}N_4O$ requires C, 76·4; H, 5·9; N, 13·7%; *M*, 410]; infrared spectrum, bands (KBr disc) at 3407, 3263 (NH), 3311, 3192 (NH, amide), 2242 (C⋮N), 1669, 1695 cm.$^{-1}$ (C=O, amide I and II).

(c) *With excess of sodium hydroxide*. The azabicyclo-octanone (2·5 g.) and ethanol (150 c.c.) containing 20% aqueous sodium hydroxide (5 c.c.) were refluxed for 3 hr. The solvent was evaporated *in vacuo*, and the residue diluted with water. Crystallisation from ethyl acetate gave 2′-hydroxy-*p*-terphenyl (1·7 g.), m. p. and mixed m. p. 194°.

(d) *With sodium hydroxide and methyl iodide*. 6% Aqueous sodium hydroxide (1 mol.) and methyl iodide (1·5 mol.) were successively added to the azabicyclo-octanone (1·0 g., 1 mol.) in ethanol (50 c.c.) and the mixture was refluxed for 3 hr., then worked up as in (c), yielding 3-cyano-2,5-diphenylcyclohex-2-en-1-one (0·5 g.), m. p. and mixed m. p. 155° (from ethyl acetate).

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(e) *Use of one equivalent of sodium hydroxide.* When experiment (d) was carried out with omission of methyl iodide the product was compound B (0·3 g.), prisms, m. p. and mixed m. p. 334—335° (from dimethylformamide).

3-Chloro-2,5-diphenylcyclohex-2-en-1-one.—2,5-Diphenylcyclohexane-1,3-dione (20·3 g.) in dry chloroform (75 c.c.) was refluxed with phosphorus trichloride (5·7 c.c.) for 2 hr. Crushed ice, ether, and aqueous sodium hydrogen carbonate were successively added and the organic layer was washed with aqueous sodium hydroxide, dried, and evaporated. The residue was recrystallised from ethyl acetate–light petroleum, yielding the *chloro-ketone* (7·0 g.) as needles, m. p. 139—140° (Found: C, 76·9; H, 5·1; Cl, 12·3. $C_{18}H_{15}ClO$ requires C, 76·4; H, 5·3; Cl, 12·5%).

The chloro-ketone (2·0 g.) and sodium cyanide (2·5 g.) in dimethylformamide (50 c.c.) were refluxed for 7 hr. Dilution of the resulting solution with water afforded 2′-hydroxy-*p*-terphenyl (80%), prisms, m. p. and mixed m. p. 194° (from ethyl acetate).

Action of Alkali on 3-Cyano-2,5-diphenylcyclohex-2-en-1-one (II).—The cyano-ketone (1·0 g.) in ethanol (50 c.c.) was refluxed with 20% aqueous sodium hydroxide (2 c.c.) for 3 hr. The ethanol was evaporated under reduced pressure, the residue diluted with water, and the product filtered off. 2′-Hydroxy-*p*-terphenyl (0·5 g.) crystallised from ethyl acetate as prisms, m. p. and mixed m. p. 194°.

1-Acetoxy-3-cyano-2,5-diphenylcyclohex-2-ene.—Potassium borohydride (1·5 g.) in water (15 c.c.) was added to 3-cyano-2,5-diphenylcyclohex-2-en-1-one (2·5 g.) in methanol (75 c.c.); the mixture was set aside for 5 hr., then poured into water, and the cyano-alcohol (2·3 g.) was filtered off, dried, and refluxed in acetic anhydride (10 c.c.) containing one drop of concentrated sulphuric acid for 1 hr. Dilution of this solution with water furnished the corresponding *acetate*, needles, m. p. 133° (from ethyl acetate–light petroleum) (Found: C, 79·3; H, 6·4; N, 4·5. $C_{21}H_{19}NO_2$ requires C, 79·5; H, 6·0; N, 4·4%).

Reaction of 3-Cyano-2,5-diphenylcyclohex-2-en-1-ol with N-Bromosuccinimide.—*N*-Bromosuccinimide (7·0 g.) and benzoyl peroxide (0·05 g.) were added to 3-cyano-2,5-diphenylcyclohex-2-en-1-ol (10·0 g.) in dry carbon tetrachloride (500 c.c.) and the mixture was refluxed for 2 hr. The precipitated succinimide was removed, and the filtrate was concentrated to an oil which solidified on trituration with benzene. Crystallisation from ethyl acetate gave *6-bromo-3-cyano-2,5-diphenylcyclohex-2-en-1-one* (4·4 g.), plates, m. p. 183° (Found: C, 64·7; H, 4·2; N, 4·1; Br, 21·3. $C_{19}H_{14}BrNO$ requires C, 64·8; H, 4·0; N, 4·0; Br, 22·7%); $\lambda_{max.}$ *215*, *225*, and 302 mμ (ε 15,300, 12,600, 3800 respectively); infrared spectrum (KBr disc), bands at 2217 (C⋮N), 1695 (α′-bromo-αβ-unsaturated C=O), and 565 cm.$^{-1}$ (C–Br). After several days, *4-bromo-3-cyano-2,5-diphenylcyclohex-2-en-1-one* (2·2 g.) crystallised from the benzene mother-liquor as yellow needles, m. p. 162° (Found: C, 64·4; H, 4·1; N, 4·0; Br, 22·8%); $\lambda_{max.}$ *214·5*, *228*, and 303 mμ (ε 15,700, 13,200, 4000 respectively); infrared spectrum (KBr disc), bands at 2208 (C⋮N), 1686 (αβ-unsaturated C=O), 534, and 522 cm.$^{-1}$ (C–Br).

*2′-Cyano-6′-hydroxy-*p*-terphenyl.*—4-Bromo-3-cyano-2,5-diphenylcyclohex-2-en-1-one (0·8 g.) in dry pyridine (5 c.c.) was refluxed for 3 hr. and then poured into dilute hydrochloric acid (200 c.c.). The solid (0·6 g.) was dried, and recrystallised from ethyl acetate, giving *2′-cyano-6′-hydroxy-*p*-terphenyl* as needles, m. p. 193° (Found: C, 83·8; H, 5·2; N, 5·3. $C_{19}H_{13}NO$ requires C, 84·1; H, 4·8; N, 5·2%); $\lambda_{max.}$ 234, 267, and 321 mμ (ε 36,900, 15,500, 9600 respectively). The same product was obtained when 6-bromo-3-cyano-2,5-diphenylcyclohex-2-en-1-one was used in place of the 4-bromo-isomer.

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329. *The Infrared Absorption of ^{18}O-Labelled Benzamide.*

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Dilute carbon tetrachloride, chloroform, and bromoform solutions of isotopically normal benzamide and benzamide containing 79 atom % of ^{18}O have been used in measurements of their spectra in the 3800—670 cm.$^{-1}$ region. The observed bands are discussed and assigned to their original vibrations. The C=^{18}O band is shifted by 24 cm.$^{-1}$ (in CCl_4), and the N–H bending (in $CHCl_3$) by 10 cm.$^{-1}$, but the C–N frequency is unaffected. The relative integrated band intensity of the C=^{18}O stretching (in CCl_4) is about 20% bigger than that of the corresponding C=^{16}O band.

The assignment of the characteristic infrared absorption bands of amides, especially those at about 1550 and 1300 cm.$^{-1}$, has been discussed very extensively,[1] being the subject of many controversies. Since the infrared absorption spectra of ^{18}O-labelled amides might, in conjunction with the normal spectra, unravel the amount of participation of the amide-oxygen atom in the vibrations associated with the various bands, we now report

Table 1. *Infrared absorption bands of benzamide, isotopically normal and containing 79 atom % of ^{18}O (optical densities in parentheses).*

No.	Species	Solvent	Concentration	Cell-thickness (mm.)	Bands (cm.$^{-1}$)
1	Normal	CCl_4	Satd. (<0·4 g./l.)	20	3540(0·12), 3420(0·14), 3160(0·10), 3080(0·09),
2	^{18}O	CCl_4	,,	20	3535(0·11), 3430(0·13), 3160(0·09), 3080(0·085),
3	Normal	$CHCl_3$	7·6 g./l.	1	3525(0·27), 3410(0·30), — [c]
4	^{18}O	$CHCl_3$	4·3 g./l.	1	3530(0·12), 3425(0·16), — [c]
1	Normal (contd.)	CCl_4	Satd. (<0·4 g./l.)		1689(1·1), [a] 1357(0·88) [b]
2	^{18}O (contd.)	CCl_4	,,		1666(1·2), [a] 1356(0·95) [b]
3	Normal (contd.)	$CHCl_3$	7·6 g./l.		1672(⩾1·5) 1584(1·2), 1368(1·2) [d]
4	^{18}O (contd.)	$CHCl_3$	4·3 g./l.		1656(1·2) 1576(0·68), 1367(0·75) [d]
	Normal [e]	$CHBr_3$	0·02 g. + 1 ml.	1·4	800(0·48), 724(0·42)
	^{18}O [e]	$CHBr_3$	0·017 g. + 1 ml.	1·4	799(0·35), 723(0·30)
	Normal [f]	CCl_4	0·138 g./l.	20	1690(0·98) 1358(0·66)
	^{18}O [f]	CCl_4	0·065 g./l.	20	1666(0·48) 1358(0·30)
	Normal [f]	$CHCl_3$	1·39 g./l.	1	1675(0·66), 1606s, 1584(0·26)
	^{18}O	$CHCl_3$	1·39 g./l.	1	1655(0·61) 1605s, 1574(0·18)

[a] The 1640—1440 cm.$^{-1}$ region is masked by the solvent. No more bands observable down to 1280 cm.$^{-1}$. [b] The 3150—3050 cm.$^{-1}$ region is masked by the solvent. [d] In the 1270—1170 cm.$^{-1}$ region and from 830 cm.$^{-1}$ downwards the chloroform absorption practically obliterates that of the solute. [e] Measured only in the 830—670 cm.$^{-1}$ region. [f] Measured precisely and only at the vicinity of the main bands.

the spectra in the 3800—670 cm.$^{-1}$ region for dilute solutions of isotopically normal benzamide and benzamide containing 78·9 ± 0·4 atom % of ^{18}O in carbon tetrachloride, chloroform, and bromoform.

[1] Jones and Sandorfy in "Technique of Organic Chemistry," Interscience Publ. Inc., New York, N.Y., 1956, Vol. IX, pp. 521—530; Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen & Co. Ltd., London, 1958, pp. 203—221; Fraser and Price, *Nature*, 1952, **170**, 490; Price and Fraser, *Proc. Roy. Soc.*, 1953, *B*, **141**, 66; Gierer, *Z. Naturforsch.*, 1953, **8b**, 644, 654; Myazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1956, **24**, 408; Becher and Griffel, *Naturwiss.*, 1956, **43**, 467; Becher, *Chem. Ber.*, 1956, **89**, 1593.

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The infrared absorption of normal benzamide has already been reported several times;[2-6] a full solution spectrum, however, has not yet been published, the reported spectra being either for a solid sample[3,5,6] or of a fragmentary nature.[2,4] Table 1 summarises our results.

The medium bands at about 3530 and 3420 cm.$^{-1}$, which belong respectively to the asymmetrical and symmetrical stretching vibrations of a free NH_2 group,[7] show that even in ~1% solution in chloroform benzamide is largely monomeric. The barely visible band at 3160 cm.$^{-1}$, although observed with a <0·003M-carbon tetrachloride solution, must however be attributed to a hydrogen-bonded NH_2 stretching vibration existing in a dimer, since its relative intensity increases with concentration.[2] A small amount of dimer thus persists even in very dilute solutions of benzamide in carbon tetrachloride.

The values found for these bands with normal benzamide solutions agree well with those (3535, 3420, and 3170 cm.$^{-1}$) reported by Buswell, Rodebush, and Roy [2] for carbon tetrachloride solutions of benzamide, with the 3520 and 3410 cm.$^{-1}$ values reported by Richards and Thompson [4] for a chloroform solution, and with a value of about 3160 cm.$^{-1}$ for the hydrogen-bonded NH_2 group in the solid state.[6]

The 3080 cm.$^{-1}$ band is clearly due to the aromatic C–H stretching vibration; Buswell and his co-workers [2] observed it at the same frequency.

The 1690 cm.$^{-1}$ band of normal benzamide in carbon tetrachloride solution must be due to the carbonyl stretching vibration of the monomeric molecule, as is shown by its much lower frequency for the ^{18}O-labelled modification. Richards and Thompson [4] observed it in this vicinity with a dioxan solution and assigned it in the same way. The value 1675 cm.$^{-1}$ given in Table 1 for a chloroform solution agrees with a reported value [8] of 1678 cm.$^{-1}$. For hydrogen-bonded solid benzamide this band appears [6] at about 1665 cm.$^{-1}$.

The strong 1584 and 1368 cm.$^{-1}$ bands of normal benzamide in chloroform solution (in solid benzamide: [6] 1630, 1410) are the well-known II amide band and the primary amide analogue of the III amide band, respectively (Myazawa *et al.*[1]). Their discussion is best deferred until after that of labelled benzamide.

The bands for bromoform solutions at 800 and 724 cm.$^{-1}$ are analogous to those for the hydrogen-bonded solid spectrum at 790, 771 (doublet), and 705 cm.$^{-1}$, respectively.[6,9] The higher bands seem to be due to the aromatic C–H out-of-plane bending vibrations of benzenes monosubstituted by an electron-accepting group [10] while the lower band is probably mainly due to the out-of-plane N–H bending (we are obliged to a Referee for this assignment).

The spectrum of the ^{18}O-labelled benzamide, as can be expected, shows no appreciable difference for the NH and C–H stretching frequencies in carbon tetrachloride or chloroform solution.

The C=O stretching frequency of [^{18}O]benzamide in carbon tetrachloride solution is decreased by 24 cm.$^{-1}$ from the normal (1690 to 1666 cm.$^{-1}$). This shift can be compared with the shift of 29 cm.$^{-1}$ for [^{18}O]benzophenone in carbon tetrachloride [11] and shows that the vibration which is responsible for the 1690 cm.$^{-1}$ band in normal benzamide is mainly concentrated in the carbonyl group. This result is somewhat at variance with the

[2] Buswell, Rodebush, and Roy, *J. Amer. Chem. Soc.*, 1938, **60**, 2444.
[3] Barnes, Liddel, and Williams, *Ind. Eng. Chem., Analyt.*, 1943, **15**, 659.
[4] Richards and Thompson, *J.*, 1947, 1248.
[5] Mann and Thompson, *Proc. Roy. Soc.*, 1948, *A*, **192**, 489.
[6] Wyandotte Chemicals Co., National Research Council Infrared Spectral Catalog, Keysort compound card no. 670.
[7] Jones *et al.*, ref. 1, p. 513.
[8] Brown, Regan, Schuetz, and Steinberg, *J. Phys. Chem.*, 1959, **63**, 1324.
[9] Margoshes and Fassel, *Spectrochim. Acta*, 1955, **7**, 14.
[10] Kross, Fassel, and Margoshes, *J. Amer. Chem. Soc.*, 1956, **78**, 1332; Jones *et al.*, ref. 1, pp. 390–391.
[11] Halmann and Pinchas, *J.*, 1958, 1703.

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calculations by Myazawa and his co-workers [1] for formamide, according to which there is a big contribution from the C–N stretching vibration to its 1688 cm.$^{-1}$ (I amide) frequency.

The II amide band is shifted in [^{18}O]benzamide from 1584 to 1574 cm.$^{-1}$ (in $CHCl_3$). The " III amide " band remains, however, almost unaffected by the isotopic substitution, at 1358 cm.$^{-1}$ (in CCl_4). The II amide band is usually,[4] at least for primary amides (Jones *et al.*, Bellamy [1]), assigned to the N–H bending mode of vibration although other modes have also been suggested as its origin (Bellamy,[1] Lenormant [12]). The decrease of 10 cm.$^{-1}$ in its frequency because of the isotopic replacement is therefore rather unexpected. It seems, then, that during the N–H bending vibration the amide-oxygen atom is also forced to move considerably because this bending affects the distribution of the bonding electrons of the whole amide group. Such a situation will explain why $CH_3{\cdot}CO{\cdot}ND_2$ does not show this band at about 1250 cm.$^{-1}$, as was expected on the assumption that the origin of this band is an N–H bending vibration,[13] since this vibration is now seen to be shared also by other parts of the molecule and cannot be expected to decrease so much on deuteration.

The " III amide " band was observed by Randall and his co-workers [14] in the spectra of solid primary amides in the 1418—1399 cm.$^{-1}$ region and was assigned to the =C–N stretching vibration, its frequency being higher in this case because of the partial double bond of this group in amides. The big difference between the solid-state value (1410 cm.$^{-1}$) and that of a carbon tetrachloride solution (1358 cm.$^{-1}$) must be attributed to the strong hydrogen bonding in the centrosymmetric dimeric solid state,[15] which opposes such a stretching vibration since the latter directly stretches this bond. The correctness of this assignment is shown by (*a*) the fact that all the tetraphenylporphins investigated show such a strong, =C–N stretching band [16] at about 1360 cm.$^{-1}$ (here also, resonance with forms having a –C=N– structure contributes to the structure of the molecule) and (*b*) the observation [17] that deuteration does not change the frequency of this band by more than 1—3 cm.$^{-1}$. Its high intensity (over 50% of that of the C=O stretching band), taken with the insensitivity to labelling with ^{18}O, also indicates its connexion with the movement of the polar nitrogen atom.

According to Myazawa *et al.*[1] the band due to that vibration in which the C–N group of formamide is stretched should appear at about 1310 cm.$^{-1}$. These authors assume that during this vibration the oxygen atom also moves considerably (the vibration being, in fact, a symmetrical stretching of the N–C=O group); hence an appreciable decrease in the frequency of the " III amide " band would have been expected in the spectrum of [^{18}O]benzamide. That this is by no means the case seems to show that because of the similarity between C–N and $C–C_{ar}$ bonds (both of partial double-bond character and between similar participants) in benzamide the vibration in which the C–N group is stretched (responsible for the 1358 cm.$^{-1}$ band) is shared by the $C–C_{ar}$ bond but only very little by the C=O linkage, the characteristic frequency of which is much higher than 1358 cm.$^{-1}$.

The higher frequency of the C–N band in chloroform solution than in carbon tetrachloride (1368 and 1367; 1358 cm.$^{-1}$) must be attributed to the increase in the polar character of the amide group due to interaction of this group with chloroform; this means a stronger partial double bond between the carbon and nitrogen.

The shoulder appearing in both spectra at about 1605 cm.$^{-1}$ is probably due to a phenyl band (at about 1595 cm.$^{-1}$ in the solid [6]) which is masked in part by the much stronger II amide band at about 1580 cm.$^{-1}$, while the phenyl band at about 1500 cm.$^{-1}$ seems to be too weak to be observed in the concentrations used for the measurements.

[12] Lenormant, *Bull. Soc. chim. France*, 1948, **15**, 33.
[13] Lenormant, *Ann. Chim.* (*France*), 1950, **5**, 459.
[14] Randall, Fowler, Fuson, and Dangl, " Infrared Determination of Organic Structures," Van Nostrand, New York, 1949, Table opposite p. 21.
[15] Penfold and White, *Acta Cryst.*, 1959, **12**, 130.
[16] Thomas and Martell, *J. Amer. Chem. Soc.*, 1959, **81**, 5111.
[17] Kniseley, Fassel, Gray, and Farquhar, personal communication.

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The Intensity of the Amide Bands in [^{18}O]*Benzamide.*—It was shown recently [11] that the molar extinction coefficient of the C=O band of [^{18}O]benzophenone is about 15% lower than that of the normal benzophenone. It was also found that for triphenylphosphine oxide both the molar extinction coefficient and the apparent relative integrated intensity of the P=^{18}O band are much lower than of the P=^{16}O band.[18] We therefore measured the

TABLE 2. *Absorption intensity of the amide bands of* $C_6H_5 \cdot C^{16}O \cdot NH_2$ *and* $C_6H_5 \cdot C^{18}O \cdot NH_2$ *(apparent half-widths, in cm.$^{-1}$, in parentheses).*

Material	Frequency (cm.$^{-1}$)	Cell-thickness (mm.)	Concn. (g./l.)	Solvent	Optical density	Mol. extinction coeff. (l. mole^{-1} cm.$^{-1}$)	Rel. integrated intensity (l. mole^{-1} cm.$^{-2}$)
Normal ...	1690	20	0·052	CCl_4	0·448	520	10,400(20)
Labelled ...	1666	20	0·065	CCl_4	0·479 [a]	580 [b]	12,800(22)
Normal ...	1358	20	0·052	CCl_4	0·234	272	3530(13)
Labelled ...	1358	20	0·065	CCl_4	0·296	280	3500(12·5)
Normal ...	1358	20	0·138	CCl_4	0·66	289	
Normal ...	1675	1	1·40	$CHCl_3$	0·664	578	14,500(25)
Labelled ...	1655	1	1·39	$CHCl_3$	0·61 [a]	690 [b]	14,500(21)
Normal ...	1584	1	1·40	$CHCl_3$	0·26	224	[c]
Labelled ...	1574	1	1·39	$CHCl_3$	0·19	213 [b]	[c]

[a] Uncorrected for the absorption of the remaining normal benzamide at this point. [b] Corrected for the lower effective concentration due to the presence of normal amide. [c] No estimation of the integrated band intensity can be made here owing to the near-by shoulder at ~1605 cm.$^{-1}$.

intensity of the amide bands of $C_6H_5 \cdot C^{16}O \cdot NH_2$ and $C_6H_5 \cdot C^{18}O \cdot NH_2$. The relative integrated band intensities were estimated by multiplying the apparent maximum molecular extinction coefficients of the bands by their half-widths (on the assumption that the form of the bands is not changed much by the isotopic exchange); these intensities are given in Table 2.

This Table shows that the intensity of the band due to the C–N stretching is practically unaffected by the isotopic exchange. The C=O stretching band, however, appears to be stronger by ~20% for [^{18}O]benzamide in carbon tetrachloride. It is true that in chloroform solution the integrated intensity is equal in both isotopic modifications but it is quite possible that in this case the interaction of the chloroform with benzamide, which is shown by, *e.g.*, the general increase in the C=O band intensity in chloroform and might be somewhat weaker for the labelled compound,* obliterates the inherent difference between the ^{18}O- and ^{16}O-amides, as shown in the carbon tetrachloride results. Anyhow, the absorption intensity of the [^{18}O]benzamide-carbonyl group in carbon tetrachloride seems again to be appreciably different from that of a similar C=^{16}O group, although this time in the opposite direction to that for benzophenone [11] and triphenylphosphine oxide: [18] the reason for this is under investigation.

EXPERIMENTAL

Normal Benzamide.—A pure sample of this compound (m. p. 126°) was prepared from benzoic acid [see method (*b*) for the labelled amide].

[^{18}O]*Benzamide.*—This compound was prepared by two methods: (*a*) Partial acid-hydrolysis of benzonitrile (8 g., freshly distilled) was effected in a solution of ^{18}O-enriched water (40 ml.) saturated with dry hydrogen chloride. The mixture was heated in a sealed tube for about 2 hr. at 100° and, after cooling, the excess of water was distilled off, and the [^{18}O]benzamide extracted with dioxan and recrystallised repeatedly from light petroleum; it had m. p. 126°. No N–D bands could be discerned in its spectrum.

(*b*) Complete hydrolysis of benzonitrile (4 g.) was achieved in ^{18}O-enriched water (30 ml.) saturated with dry hydrogen chloride in a sealed tube for 24 hr. at 100°. The [^{18}O]benzoic acid was separated, recrystallised from ether, and treated with a slight excess of thionyl chloride. Fractional distillation gave [^{18}O]benzoyl chloride, b. p. 198°/760 mm., that was aminated in

* As suggested by the difference between the half-width of the C=^{16}O band (25 cm.$^{-1}$) and that of the C=^{18}O band (21 cm.$^{-1}$), in chloroform.

[18] Halmann and Pinchas, *J.*, 1958, 3264.

dioxan by passing in dry ammonia (ice-cooling) until saturated. The ammonium chloride formed was filtered off, the dioxan removed, and the [^{18}O]benzamide recrystallised from dioxan–light petroleum and washed with hexane; the amide then had m. p. 126°.

Isotopic-oxygen analyses were done by the method of Anbar and Gutmann [19] as described by Samuel.[20]

Infrared Measurements.—The instrument was a Perkin–Elmer, model 12C, spectrophotometer with a sodium chloride prism. Its calibration was checked daily by using atmospheric water vapour as standard. In each case the spectrum of the solvent was run in the same cell immediately before the spectrum of the measured solution. The intensity measurements were carried out in duplicate and in this case the spectra contained only the vicinity of the measured bands; the mean difference between the optical density of the solution and that of the solvent at each point was taken as the true optical density of the solution there. The slit used in the 1700—1550 cm.$^{-1}$ region was about 0·12 mm. The normal and the corresponding labelled spectrum were generally run one after the other in the same cell.

We thank Mr. J. Goldberg for carrying out the infrared measurements.

THE WEIZMANN INSTITUTE OF SCIENCE,
REHOVOTH, ISRAEL. [*Received, July 22nd,* 1960.]

[19] Anbar and Gutmann, *Internat. J. Appl. Radn. Isotopes,* 1959, **4**, 234.
[20] Samuel, *J.*, 1960, 1318.

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330. *Sulphates of Monosaccharides and Derivatives. Part II.*[1] *Periodate Oxidation.*

By J. R. TURVEY, M. J. CLANCY, and T. P. WILLIAMS.

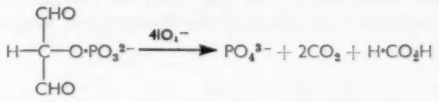
The oxidation with periodate of glucose 3- and 6-sulphate and of galactose 6-sulphate has been studied under various conditions of pH; the results are compared with the oxidations of the analogous phosphates. The monosulphate prepared by direct sulphation of methyl β-D-galactopyranoside has been shown by periodate oxidation to be the 6-sulphate.

SUGAR SULPHATES are difficult to characterise since few of these salts have definite melting points and they do not readily form crystalline derivatives. Paper chromatography can be used to differentiate between certain isomeric sulphates [1,2] but other methods for their characterisation seemed desirable.

The use of periodate oxidation in structural investigations of carbohydrates is well established but there are few reports on its reaction with carbohydrate sulphates. Barry, Dillon, and their co-workers [3] used this reagent in structural investigations of a number of sulphated polysaccharides from algæ and assumed that the sulphate groups are stable to the reagent. Holt [4] briefly reported that the sulphate groups in some sugar sulphates are liberated on periodate oxidation but are stable in other cases. The reactions of the analogous sugar phosphates with periodate have, however, received considerable attention. Reducing sugar phosphates are usually considered as being oxidised in ring form with production of intermediate formyl esters [5,6] but the consumption of periodate and the end products of the reaction depend on the conditions of the reaction and on the position of the phosphate group. Ribose 5-phosphate and glucose 6-phosphate consume 3 and

[1] Part I, *J.*, 1960, 4761.
[2] Dodgson and Spencer, *Biochem. J.*, 1954, **57**, 310; Lloyd, *Nature*, 1959, **183**, 109; Rees, *Nature*, 1960, **185**, 309.
[3] Barry and Dillon, *Proc. Roy. Irish Acad.*, 1945, **50***B*, 349; Dillon and O'Colla, *ibid.*, 1951, **54***B*, 51; Barry and McCormick, *J.*, 1957, 2777.
[4] Holt, Inst. Seaweed Res., Ann. Reports for 1958, p. 15.
[5] Morrison, Rouser, and Stotz, *J. Amer. Chem. Soc.*, 1955, **77**, 5156.
[6] Loring, Moss, Levy, and Hain, *Arch. Biochem. Biophys.*, 1956, **65**, 578; but see Distler, Merrick, and Roseman, *J. Biol. Chem.*, 1958, **230**, 497.

4 mol. of periodate, respectively, and give the relatively stable glycollaldehyde phosphate [7-10] although, at pH 8, this ester is slowly hydrolysed to inorganic phosphate and glycollaldehyde, which is then further oxidised.[7] Glucose 2-, 3- and 4-phosphate and ribose 2- and 3-phosphate are all oxidised to the same intermediate tartrondialdehyde phosphate (I). This then undergoes overoxidation to yield inorganic phosphate, carbon dioxide and formic acid, with the consumption of 4 mol. of periodate: [8]

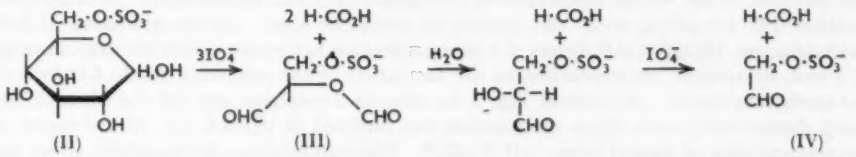


(I)

We now report a comparative study of the periodate oxidation of synthetic sugar sulphates [1] and of sugar phosphates.

To avoid the precipitation of insoluble barium salts, the sugar sulphates were used as either sodium or potassium salts. Oxidations were carried out with an excess of sodium metaperiodate either in unbuffered (initial pH 4·2—4·8) or in buffered solution. In the former case, both the consumption of periodate and the liberation of formic acid were measured but, in the latter cases, only the consumption of periodate was determined. Under alkaline conditions, a lower concentration of the periodate was used in order to prevent precipitation of disodium paraperiodate [11] and, with the same object, potassium salts of the sugar sulphate and buffers were preferable.

The oxidation of galactose 6-sulphate and of glucose 6-sulphate in an unbuffered solution (pH 4·2 falling to 3) followed the course shown in Fig. 1. With each sulphate there was an initial rapid (1 hr.) consumption of over 3 mol. of periodate with the liberation of 2 mol. of formic acid, the latter rising to 3 mol. after a few hours, and finally both the periodate consumption and formic acid liberation became constant at about 3·5 mol. An oxidation sequence such as that depicted for glucose 6-sulphate (II) would require the rapid consumption of 3 mol. of oxidant and the liberation of 2 mol. of acid with the formation of 2-*O*-formylglyceraldehyde 3-sulphate (III). Hydrolysis of the formyl ester, which is relatively slow at pH 4,[12] would be followed by further oxidation to glycollaldehyde sulphate (IV), in which 1 mol. of periodate is consumed and 2 mol. of formic acid are liberated. Neither the periodate consumed nor the formic acid liberated reached the theoretical values of 4 mol., but similar incomplete oxidation has been reported for ribose 5-phosphate in unbuffered solution, which consumes only 2·5 instead of 3 mol. of oxidant.[7] Explanations, based on the stability of the intermediate formyl ester,[7] do not, however, agree with the fact that, in the case of the hexose 6-sulphates the formic acid liberated was equivalent to the oxidant ultimately consumed. Loring *et al.*[9] have shown that, at neutral pH, ribose 5-phosphate consumes the expected 3 mol. of periodate. In phosphate buffer at pH 6·6, the 6-sulphates of glucose and galactose consumed 3·87 and 3·82 mol.



(II) (III) (IV)

of oxidant respectively. In an alkaline buffer (borate, pH 8·2) approximately the same figures were obtained although uptake of oxidant was faster, presumably owing to faster

[7] Marinetti and Rouser, *J. Amer. Chem. Soc.*, 1955, **77**, 5345.
[8] Courtois and Ramet, *Bull. Soc. Chim. biol.*, 1945, **27**, 610.
[9] Loring, Levy, Moss, and Ploeser, *J. Amer. Chem. Soc.*, 1956, **78**, 3724.
[10] Khym, Doherty, and Cohn, *J. Amer. Chem. Soc.*, 1954, **76**, 5523.
[11] Jeanloz and Forchielli, *J. Biol. Chem.*, 1951, **188**, 361.
[12] Neumüller and Vasseur, *Arkiv Kemi*, 1953, **5**, 235.

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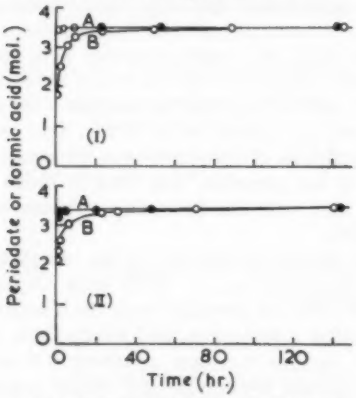
hydrolysis of the formyl esters in alkaline media. Bicarbonate buffer (pH 7·8), which is reported as favouring complete oxidation,[13] did not further increase the consumption of periodate. In no case did the consumption of periodate exceed 4 mol., thus clearly demonstrating that the glycollaldehyde sulphate is more stable to hydrolysis than glycollaldehyde phosphate, which is stable at neutral or slightly acid pH (refs. 8—10, 14) but is slowly hydrolysed at pH 8 (ref. 7). The stability of the ester link of glycollaldehyde sulphate was also indicated by the fact that no inorganic sulphate could be detected in the products of oxidation of either of the 6-sulphates, even after 216 hr. at pH 8·2.

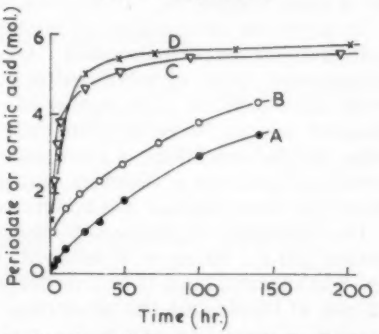
FIG. 1. *Oxidation of sugar sulphates with sodium metaperiodate.*



(I) *Galactose 6-sulphate*; (II) *Glucose 6-sulphate.*

A, *Periodate consumed*; B, *Formic acid liberated.*

FIG. 2. *Oxidation of glucose 3-sulphate with sodium metaperiodate.*

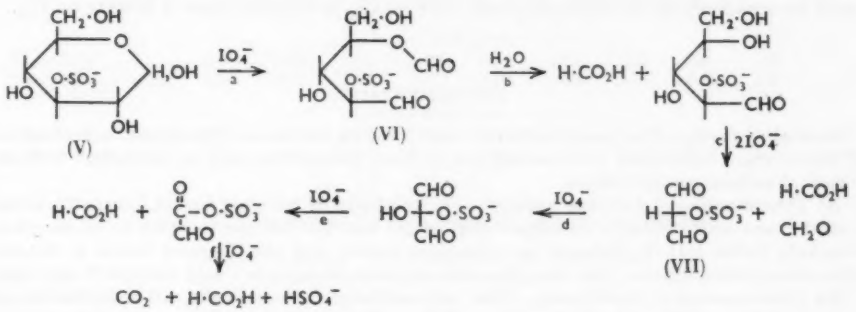


A, *Formic acid liberated in unbuffered solution*; B, *Periodate consumed in unbuffered solution*; C, *Periodate consumed in borate buffer* (pH 8·2); D, *Periodate consumed in bicarbonate buffer* (pH 7·8).

The oxidation of glucose 3-sulphate followed the course shown in Fig. 2. In unbuffered solution, 1 mol. of periodate was rapidly consumed with the liberation of very little formic acid and thereafter the oxidation proceeded slowly until, at 140 hr., over 4 mol. of oxidant had been consumed and over 3 mol. of formic acid liberated. The discontinuity of the curve after the consumption of 1 mol. of oxidant was not as sharp as was expected. The sequence of reactions a ⟶ f is suggested for the oxidation of the 3-sulphate (V). This would require rapid consumption of 1 mol. of oxidant (reaction a) and then a slow further consumption as the 4-*O*-formylarabinose 2-sulphate (VI) was hydrolysed. In unbuffered solution (pH 4·8 falling to 3) this hydrolysis would be slow. In the oxidation of 3-*O*-methylglucose, Hough *et al.*[15] observed a sharp inflection in the curve after the consumption of 1 mol. of oxidant, corresponding to the formation of the relatively stable 4-*O*-formyl-2-*O*-methylarabinose. As seen in Fig. 3 for glucose 3-sulphate, we did not observe this sharp discontinuity even when the solution was buffered at pH 3·6, *i.e.*, in the region of greatest stability of formyl esters (pH 3—5).[12] Two explanations are possible: either the sulphuric hemiester group promotes the hydrolysis of the formyl ester[4] or the molecule is not being oxidised entirely in the pyranose form, a proportion being oxidised in the open-chain form. In alkaline buffer (borate, pH 8·2) there was no discontinuity in the

[13] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580; Jeanloz, *Helv. Chim. Acta*, 1944, **27**, 1509.
[14] Euler, Karrer, and Becker, *Helv. Chim. Acta*, 1936, **19**, 1060; Kiessling and Meyerhof, *Biochem. Z.*, 1938, **296**, 410.
[15] Hough, Taylor, Thomas, and Woods, *J.*, 1958, 1212.

region of 1 mol. of oxidant consumed, the curve smoothly approaching a limiting value of 6 mol. of periodate. The use of bicarbonate buffer at pH 7·8, to favour complete oxidation,[13] gave essentially the same results as the borate buffer. If the oxidation follows the sequence depicted in reactions a ⟶ f, then at the " half-way stage " [the



tartrondialdehyde sulphate (VII) stage] the amount of oxidant consumed and formic acid liberated would be 3 and 2 mol., respectively, and this 3 : 2 ratio is observed in the unbuffered solution (*ca.* 55 hr.). The final stages of the oxidation (reactions d ⟶ f) represent a normal overoxidation although the course may not be exactly as depicted. These reactions should result in an uptake of 3 mol. of periodate and the liberation of inorganic sulphate and are in contrast to the analogous oxidation of tartrondialdehyde phosphate, during which 4 mol. of periodate are consumed.[8] In the borate buffer after 100 hr., over

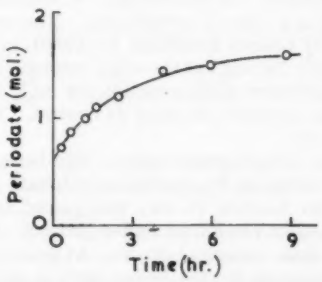
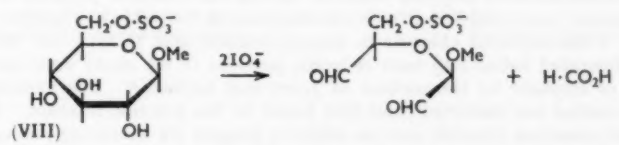


FIG. 3. *Oxidation of glucose 3-sulphate with sodium metaperiodate in acetate buffer* (pH 3·6).

80% of the sulphate had been liberated when 5·4 mol. of periodate had been consumed, and in bicarbonate buffer after 49 hr. the corresponding figures were 70% sulphate liberated and 5·35 mol. of periodate consumed. In no case was there any evidence that the total consumption of periodate would exceed 6 mol. and, indeed, the final stages of the oxidation were so slow that it was not possible to follow the consumption of periodate even to 6 mol.



Direct sulphation of methyl β-D-galactopyranoside and separation of the products has given a monosulphate as the main product.[1] By analogy with the sulphation of monosaccharides, this product should be methyl β-D-galactopyranoside 6-sulphate (VIII) and

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it was of interest to see if this compound would be oxidised by periodate in the expected manner. On oxidation this glycoside sulphate consumed 2 mol. of periodate with the liberation of 1 mol. of formic acid in 30 min. and thereafter underwent little further oxidation, in agreement with the predicted values. This result confirms the assignment of the sulphate group to the 6-position in this glycoside sulphate, since only 1 mol. of oxidant would be consumed if the sulphate group were on $C_{(2)}$ or $C_{(4)}$ and none if it were on $C_{(3)}$.

Experimental

General Methods.—The sugar sulphates were dried *in vacuo* over phosphoric anhydride at 60° before use. Oxidations were carried out at room temperature and in darkness,[16] with *ca.* 10 mol. of sodium metaperiodate.

(a) *Determination of periodate reduced.* For sulphates of reducing sugars, Linstedt's buffer method [17] was used, whereby an aliquot part of the reaction mixture is added to an excess of phosphate buffer (pH 7), followed by potassium iodide, and the liberated iodine is titrated with sodium thiosulphate. For the glycoside sulphate, Malaprade's acid method [18] was used.

(b) *Determination of formic acid.* This was estimated iodometrically, after destruction of the excess of periodate with ethylene glycol.[18]

Oxidation of Reducing-sugar Sulphates.—(a) *Unbuffered solution.* To the barium salt of the sugar sulphate (250 mg.) in water (10 ml.) was added 8% aqueous sodium sulphate (2 ml.), and the mixture was shaken. After centrifugation, the supernatant solution (10 ml.) was pipetted into the reaction flask, together with 0·3M-sodium metaperiodate (20 ml.), 0·01N-acetic acid (8 ml.), and water to 50 ml. At suitable time intervals, portions (1 ml. each) were removed, added to a mixture of 0·5M-phosphate buffer (pH 7·0; 5 ml.) and 10% aqueous potassium iodide (1 ml.), and the iodine was titrated with 0·05N-sodium thiosulphate. Other portions (2 ml. each) were added to ethylene glycol (0·5 ml.) and, after 5 min., the formic acid was determined iodometrically. A solution containing the reagents but no sugar sulphate was used as a control in each case. The results are given in Figs. 1 and 2.

(b) *Glucose 3-sulphate in acetate buffer.* The reaction mixture contained the sodium salt (5 ml.; 100 mg.) of the sugar sulphate (prepared as above), 0·2M-acetate buffer (pH 3·6; 5 ml.), 0·3M-sodium metaperiodate (10 ml.), and water to 25 ml. A similar mixture containing no sugar sulphate was used as control. The consumption of periodate was determined as above (Fig. 3).

(c) *In phosphate buffer.* The barium salt of the sugar sulphate (40 mg.) in water (5 ml.) was added to 3% potassium sulphate (1 ml.) and, after mixing and centrifugation, the supernatant solution (5 ml.) was placed in the reaction flask. The other reactants were 0·2M-potassium phosphate buffer (pH 6·6; 10 ml.), 0·15M-sodium metaperiodate (5 ml.), and water to a final volume of 50 ml. At intervals, portions (3 ml. each) were withdrawn for estimation of periodate by the buffer method as above. A control solution, containing all the reagents except the sugar sulphate, was similarly treated. The results are given in Table 1.

(d) *In borate buffer.* The reaction mixture contained the sugar solution (5 ml.) as above, 0·2M-borate buffer (pH 8·2; 25 ml.), 3% aqueous potassium sulphate (1 ml.), 0·15M-sodium metaperiodate (5 ml.), and water to 100 ml. A similar solution, containing the reagents but no sugar sulphate, was used as control. The consumption of periodate was determined as for the phosphate buffer (Table 2 and Fig. 2).

For the determination of sulphate liberated during the reaction, portions (5 ml. each) of the reaction mixture were removed at intervals and to each was added 10% aqueous potassium iodide (1 ml.), 0·45M-stannous chloride in 2N-hydrochloric acid (1 ml.) and water to 10 ml. When all the liberated iodine had been reduced, portions (1 ml. each) were removed for the determination of sulphate by the method of Jones and Letham.[19] The amount of sulphate present in the control was deducted from that found for the reaction mixture. Previous tests had shown that stannous chloride was an effective reagent for removing iodine liberated by

[16] Head and Hughes, *J.*, 1952, 2046.
[17] Lindstedt, *Arkiv Kemi, Min. Geol.*, 1945, **20***A*, No. 13.
[18] Malaprade, *Bull. Soc. chim. France*, 1926, **39**, 325; 1928, **43**, 683.
[19] Jones and Letham, *Chem. and Ind.*, 1954, 662.

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periodate and iodate, both of which interfere with the method for determining sulphate. In the cases of glucose 6-sulphate and of galactose 6-sulphate, no liberation of sulphate could be detected, but for glucose 3-sulphate the results are given in Table 2.

TABLE 1. *Consumption of periodate by sugar sulphates at* pH 6·6.

	Galactose 6-sulphate.									
Time (hr.)	0·10	0·20	0·50	1·33	4·17	6·25	24	48	72	
Consumption (mol.)	2·90	3·42	3·55	3·62	3·62	3·66	3·76	3·81	3·87	
	Glucose 6-sulphate.									
Time (hr.)	0·10	0·25	0·50	0·9	2·5	5·5	7·0	24	72	125
Consumption (mol.)	2·5	3·21	3·37	3·44	3·44	3·48	3·51	3·57	3·70	3·82

TABLE 2. *Oxidation of sugar sulphates in alkaline solutions.*

	Galactose 6-sulphate. (*Consumption of periodate in mol.*)								
Time (hr.)	0·06	0·47	1·6	3·0	18·1	22·0	48	91·5	216
Borate buffer	—	3·48	3·46	3·5	—	3·61	3·64	—	3·88
Bicarbonate buffer...	1·39	3·70	3·85	3·84	3·85	—	3·91	3·93	—
	Glucose 6-sulphate. (*Consumption of periodate in mol.*)								
Time (hr.)	0·20	0·50	1·0	3·0	24	72	164	240	
Borate buffer	3·20	3·27	3·31	3·40	3·41	3·53	—	3·91	
Bicarbonate buffer...	2·40	3·19	3·51	3·57	—	3·70	3·72	—	
	Glucose 3-sulphate. (*Liberation of sulphate as % of total.*)								
Time (hr.)	0·08	0·20	6·0	22·3	48·6	100			
Borate buffer	0	—	38	—	—	88			
Bicarbonate buffer...	—	1·5	19	53	70	—			

TABLE 3. *Oxidation of methyl* β-D-*galactopyranoside sulphate by sodium metaperiodate.*

Time (hr.)	0·15	0·25	0·50	1·0	1·5	14·5
Periodate consumed (mol.) ...	1·78	—	2·08	2·08	2·08	2·09
Formic acid liberated (mol.)	—	0·73	0·84	0·97	0·93	1·29

(e) *In bicarbonate buffer.* The conditions were as for the oxidations in borate buffer except that the borate buffer was replaced by N-potassium hydrogen carbonate (5 ml.), giving pH 7·8 in the reaction mixture. The results are given in Fig. 2 and Table 2.

Oxidation of Methyl Galactoside Sulphate.—The ammonium salt (60 mg.) was oxidised in 0·049M-sodium metaperiodate (25 ml.). At intervals, portions (0·5 ml. each) were added to 2·5% aqueous potassium iodide (2 ml.) and 3N-sulphuric acid (2 ml.) for the determination of the consumption of periodate by the acid method. Portions (2 ml. each) were also removed at intervals for the determination of formic acid. The results are given in Table 3.

We thank the National University of Ireland for the award of the Travelling Studentship in Chemistry of 1955 (to M. J. C.) and the Department of Scientific and Industrial Research for a maintenance grant (to T. P. W.).

CHEMISTRY DEPARTMENT, UNIVERSITY COLLEGE OF NORTH WALES,
BANGOR, CAERNARVONSHIRE. [*Received, September 19th,* 1960.]

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331. *Transamination. Part I. The Isolation of the Apoenzyme of Glutamic–Aspartic Transaminase from Pig Heart Muscle.*

By Barbara E. C. Banks and C. A. Vernon.

A procedure for the preparation, in quantity, of the apoenzyme of glutamic–aspartic transaminase from pig heart muscle is described. The final preparation had a higher specific activity than any previously reported for either the holoenzyme or the apoenzyme, and free-flow electrophoresis showed it to be, with respect to this technique, homogeneous. Convenient methods for following the transamination are described. Some properties of the apoenzyme are discussed.

In order to carry out chemical and kinetic studies on glutamic–aspartic transaminase and to investigate the binding between cofactor and apoenzyme we required a procedure for the preparation of relatively large quantities of apoenzyme in a homogeneous state. This paper describes such a procedure.

In the earliest studies of the purification of this enzyme, by Green, Leloir, and Nocito,[1] Schlenk and Fisher,[2] and O'Kane and Gunsalus,[3] yields and purification factors (11, 17, and 26, respectively) were relatively low and only O'Kane *et al.* achieved full resolution (*i.e.*, dissociation into apoenzyme and pyridoxal 5'-phosphate). Free-flow electrophoresis (phosphate buffer, pH 7·4) showed three components in the preparations of Green *et al.* and of Schlenk and Fisher. Both groups reported that activity was associated with two of the components.

Cammarata and Cohen[4] suggested that resolution results in partial, irreversible inactivation of the apoenzyme and described a procedure for the purification of the holoenzyme. The specific activity * (S.A.) of their final preparation, however, appears to be no greater than that of preparations obtained by the method of O'Kane and Gunsalus. Free-flow electrophoresis in phosphate (pH 7·4), and in barbiturate buffer (pH 8·6) showed the presence of three components in each preparation. It was reported, however, that, whereas in phosphate buffer two of the components contained transaminase activity, in barbiturate buffer only one was active.

An electrophoretically homogeneous preparation of the holoenzyme was obtained by Lis[5] who used zone-electrophoresis as the final step. However, comparison with our results (see below) indicates that the specific activity of this preparation (*ca.* twice that reported by Cammarata and Cohen [4]) is low and considerable inactivation must, consequently, have occurred in her purification. The most successful method for the preparation of the holoenzyme appears to be that described by Jenkins, Yphantis, and Sizer.[6] Free-flow electrophoresis showed their sample to contain 87% of the holoenzyme and comparison with our data indicates that no extensive inactivation occurs during their purification.

Detailed comparison, in terms of specific activities, of our preparation with those obtained by other workers is made, where possible, in the discussion section.

Experimental

Materials.—L-Aspartic and L-glutamic acids (Roche Products Ltd.) were chromatographically homogeneous: at 280 mμ, $\varepsilon = 0{\cdot}1$ and $0{\cdot}4$ respectively (phosphate buffer, 0·1M, pH 7·38). α-Oxo-glutaric acid, recrystallised four times from acetone–benzene, had m. p.

* We use this term to mean the catalytic activity, expressed in suitable, arbitrary, units, of any given preparation, per mg. by weight of protein.

[1] Green, Leloir, and Nocito, *J. Biol. Chem.*, 1945, **161**, 559.
[2] Schlenk and Fisher, *Arch. Biochem.*, 1947, **12**, 69.
[3] O'Kane and Gunsalus, *J. Biol. Chem.*, 1947, **170**, 425.
[4] Cammarata and Cohen, *J. Biol. Chem.*, 1951, **193**, 53.
[5] Lis, *Biochim. Biophys. Acta*, 1958, **28**, 191.
[6] Jenkins, Yphantis, and Sizer, *J. Biol. Chem.*, 1959, **234**, 51.

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114°, and ε 28 at 280 mμ (phosphate buffer, 0·1M, pH 7·38). Oxaloacetic acid, recrystallised three times from boiling ethyl acetate, had m. p. 151° (decomp.). In tris(hydroxymethylamino)methane buffer (0·0667M) of pH 7·4 or 8·3, and in phosphate buffer (0·1M) of pH 7·38, ε = 625, 635, and 550, respectively, at 280 mμ; in borate buffer (0·03M) of pH 9·2, ε = 1730 at 270 mμ.

Pyridoxal 5′-phosphate (Roche Products Ltd.) had $\lambda_{max.}$ 325, 388 mμ (ε 2860, 5180) in phosphate buffer (0·1M, pH 7·38). Pyridoxamine 5′-phosphate (Californian Foundation for Biochemical Research), had $\lambda_{max.}$ 253, 326 mμ (ε 5250, 9800) in phosphate buffer (0·1M, pH 7·38). Calcium phosphate gel was prepared as described by Dixon and Webb.[7]

Pig's hearts were obtained from Wall's Bacon Factory and were either used immediately or stored at −20°. Fatty and vascular tissue was removed before use.

L-Glutamic decarboxylase was obtained from *E. coli* (NCTC 8548). The organisms were grown at 37° on a medium containing lab. lemco (1%), peptone (1%), sodium chloride (0·5%), and L-glutamic acid (0·5%). The cells were harvested after 18 hours' growth, and an acetone powder was prepared from them in the usual way. A standard solution of L-glutamic acid (10^{-5} mole) was completely decarboxylated in 15 min. (pH 5·0) by 0·5 c.c. of a 2% suspension of the acetone powder in water.

Assay Methods.—Two methods were used, both based on the fact that oxaloacetic acid has a higher absorption in the region 280 mμ than any of the other reaction components.

Method 1.* A freshly prepared solution (22 c.c.) of sodium aspartate, α-oxoglutaric acid, and phosphate buffer (0·1M, pH 7·38) was allowed to reach thermal equilibrium in a thermostat bath (25°). A solution (2 c.c.), also at 25°, of activated enzyme and phosphate buffer (0·1M, pH 7·38) was added to start the reaction. Aliquot parts (5 c.c.) were withdrawn at appropriate times (all within 10 min. from time zero), and run into standard flasks (10 c.c.) containing 30% trichloroacetic acid (0·5 c.c.). After addition of 0·5M-sodium hydroxide (sufficient to neutralise the trichloroacetic acid) and borate buffer (2 c.c.; 0·3M, pH 9·4), the contents of the flask were made up to the mark. The flasks were left for $\geqslant$10 min. (thus minimising errors due to decarboxylation of oxaloacetic acid), and the optical densities of the solutions at 270 mμ were determined in a 1 cm. cell using a Unicam spectrophotometer (S.P. 500). It was shown that the absorption of oxaloacetic acid in borate buffer obeys Beer's law up to concentrations of *ca.* 5×10^{-4}M, and also that the decarboxylation of oxaloacetic acid is negligibly slow under all relevant conditions.

The unit of enzyme activity is defined as that amount of enzyme which, under the standard conditions described above and with concentrations of sodium aspartate and α-oxoglutaric acid of, $8{\cdot}3 \times 10^{-3}$M and $2{\cdot}08 \times 10^{-3}$M, respectively, produces, in 10 min., an amount of oxaloacetic acid corresponding to an increase in the optical density of the final solution of 0·10. This increase in optical density corresponds to the production of $1{\cdot}40 \times 10^{-4}$M-oxaloacetic acid in the assay mixture, and is *ca.* 13% of the increase expected at complete reaction (calculated from the value of the equilibrium constant given below). Experiments showed that, under the above conditions, the reaction rate is independent of time up to *ca.* 20% reaction. The initial reaction rate (v'), therefore, can conveniently be found from the linear portion of a plot of optical density against time. Consequently, the amount of enzyme used in each experiment was chosen so that the increase in optical density at the longest time interval was less than 0·16 (*i.e.*, less than $2{\cdot}2 \times 10^{-4}$M-oxaloacetic acid produced).

The following experiment is illustrative. An enzyme solution (total protein 3·55 mg. c.c.$^{-1}$) was diluted (1 : 1000), and then assayed:

t (min.)	2·0	4·5	7·0	9·5
O.D. (270 mμ)	0·237	0·257	0·278	0·298

This gives $v' = 0{\cdot}0082$ O.D. unit min.$^{-1}$. The undiluted enzyme solution, therefore, contained 820 units c.c.$^{-1}$; specific activity 231.

It was established that, under the above assay conditions, v' is proportional to enzyme concentration (E), providing that this does not exceed *ca.* 0·1 unit c.c.$^{-1}$ (in the assay solution).†

* This is a modification of the method first introduced by Greenwood and Greenbaum.[8]

† At higher concentrations v' increases less rapidly than E. The functional dependence is, however, complicated and involves the substrate and the buffer concentration. This problem will be discussed in a later publication.

[7] Dixon and Webb, "The Enzymes," Longmans, Green and Co., London, 1958, p. 51.

[8] Greenwood and Greenbaum, *Biochim. Biophys. Acta*, 1953, **10**, 623.

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Method 2. The mixture (substrates and enzyme in phosphate buffer of 0·1M, pH 7·38) was placed in a 1 cm. cell and the change in optical density recorded by using a Cary recording spectrophotometer. The control solution contained all the components except sodium aspartate. The reaction was initiated, as in method 1, by addition of the enzyme solution to a solution containing all the other components. For experiments of short duration, effective temperature control (25°) can be achieved by bringing the solutions to temperature in a thermostat-bath before initiation of the reaction. For experiments of longer duration a thermostatically-controlled cell-holder must be used. Readings could be obtained within 30 sec. of time zero. The initial reaction rate was found, as before, from the linear portion of the plot of optical density against time. A typical experiment (25°), with 10^{-2}M-sodium aspartate and $2·5 \times 10^{-3}$M-α-oxoglutaric acid, gave the data:

t (min.)	0·50	0·67	0·83	1·00	1·33	1·67	2·0	2·5	3·0
O.D. (280 mμ).....	0·042	0·056	0·071	0·085	0·111	0·135	0·156	0·184	0·208

The first five points lie on a straight line which passes through the origin; hence $v' = 0·084$ O.D. unit min.$^{-1}$.

To convert values of v' (optical density unit min.$^{-1}$) into values of v [mole l.$^{-1}$ (of oxaloacetic acid) min.$^{-1}$], the appropriate molar extinction coefficients (given above) of oxaloacetic acid and α-oxoglutaric acid must be used. The two assay methods gave, substantially, the same values of v. Table 1 illustrates with data obtained at 25° with sodium aspartate (10^{-2}M), α-oxoglutaric acid ($2·5 \times 10^{-3}$M), and phosphate buffer (0·1M, pH 7·38).

TABLE 1. *Comparison of assay methods.*

Enzyme solution (c.c.)	0·1	0·05	0·025	0·01	0·0025
$10^4 v$ { method 1	3·86	2·64	1·84	1·06	0·33
{ method 2	3·78	2·55	1·72	1·00	0·32

Determination of Protein Concentration.—Routine protein determinations were made by measuring the absorption of buffered solutions (0·1M-phosphate, pH 7·38) against a control of the buffer solution, at 280 mμ in 1 cm. cells. The relation between absorbancy and dry weight (R = mg. c.c.$^{-1}$ O.D. unit^{-1}) was determined for samples at different stages in the purification procedure by drying to constant weight (at 100°) solutions of known absorbancy which had been exhaustively dialysed:

S.A. (unit mg.$^{-1}$)	275	420	610	700
R	1·04	0·86	0·79	0·74

Reactivation of Apoenzyme.—Preparations of the apoenzyme (*ca.* 1 unit c.c.$^{-1}$) were activated (25°; 0·1M-phosphate buffer, pH 7·38) by addition of pyridoxal 5′-phosphate ($7·5 \times 10^{-5}$M) or of pyridoxamine 5′-phosphate ($3·75 \times 10^{-4}$M). It was established that (*a*) complete activation occurred within 30 min., (*b*) the level of activity reached was independent of which cofactor was used, (*c*) no loss of activity occurred on subsequent dilution or change of pH, and (*d*) the level of activity obtained by activating concentrated solutions and then diluting them was the same as that obtained by activation after dilution.

Resolution of Holoenzyme.—Loss of cofactor is virtually complete if the holoenzyme is heated at 60° for 50 min. in 1·0M-phosphate buffer at pH 6·0. Since the enzyme is thermally more stable in concentrated solution, the resolution step was normally carried out (after dialysis) on the concentrated solution obtained after the first ammonium sulphate treatment (*i.e.*, from step 2 of the procedure given below). Experiments showed that all the activity present in the original solution could be restored, after resolution, by activation with pyridoxal 5′-phosphate as described above.

Estimation of L-*Glutamic Acid.*—The following procedure was used to estimate L-glutamic acid in mixtures containing oxaloacetic acid, α-oxoglutaric acid, L-aspartic acid, and transaminase. An aliquot part (5 c.c.) was run into 30% trichloroacetic acid (0·5 c.c.), and the mixture set aside for 5 min. After neutralisation with 0·5M-sodium hydroxide, sufficient acetate buffer (0·5M, pH 4·5) was added to bring the volume to 10 c.c. An aliquot part (5 c.c.) of the resulting solution was placed in a Warburg flask containing 0·5 c.c. of an active, cell-free

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solution of L-glutamic decarboxylase in the side-arm. When thermal equilibrium (25°) was reached the reaction was started; evolution of carbon dioxide was measured for about 1 hr. With highly active L-glutamic decarboxylase nearly all the L-glutamic acid was decomposed within a few minutes, but it was necessary to take readings for longer in order to correct for the slow decarboxylation of oxaloacetic acid. Extrapolation to zero time of the final, linear portion of the plot of volume of gas evolved against time gives the volume of carbon dioxide produced from the L-glutamic acid (see Fig. 1).

Purification of the Apoenzyme.—Ammonium sulphate fractionations were carried out by slow addition of the solid to cooled solutions. Ethanol fractionations were carried out with careful temperature control (below 0°) and efficient stirring. Untreated Visking tubing was used for dialysis of solutions obtained from the early steps. For dialysis of solutions of the highly purified enzyme, Visking tubing was left for 24 hr., first, in 50% aqueous ethanol, secondly, in a solution containing EDTA (10^{-4}M) and glutathione (10^{-4}M).

Step 1. Sliced muscle was homogenized with water (weight ratio 1 : 5) in an M.S.E. Ato-Mix at maximum speed for 2 min. The suspension was stirred at 0° for 1 hr. and then centrifuged.

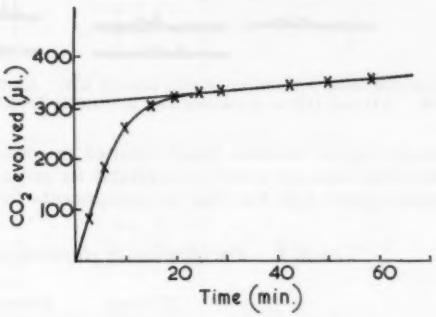


FIG. 1. *Decarboxylation of L-glutamic acid.*

Step 2. Ammonium sulphate (to 90% saturation; all percentages refer to 25°) was added to the solution and the precipitate removed, then dissolved in the *minimum* quantity of water and dialysed against running tap water until all the ammonium sulphate had been removed.

Step 3. Phosphate buffer (to M, pH 6·0) was added and the solution heated with occasional shaking for 50 min. in a water-bath at 60°. The precipitate was removed. The filtrate was used directly for step 4 (*i.e.*, without dialysis). Resolution of the enzyme was, at this point, virtually complete.

Step 4. The protein was fractionally precipitated with ammonium sulphate. The fraction 0—30% was discarded and the fractions 30—35, 35—40, and 40—45% were collected, dissolved in the minimum volume of water, dialysed, and then assayed. Fractions with S.A. > 75 were combined.

Step 5. Step 4 was repeated. The fraction 0—50% was discarded and the fractions 50—52·5, 52·5—57·5, and 57·5—60% were collected and treated as above. Fractions with S.A. > 100 were combined.

Step 6. Calcium phosphate gel was added to the combined active fractions from (5) and the whole was left for 5 min. before centrifugation. Only inactive protein is to be absorbed in this step and it is necessary to carry out pilot experiments to determine the optimum volume of gel. In general, the gel absorbed *ca.* 10 mg. of protein per c.c. The enzyme concentration in the supernatant layer must not, for stability reasons, be allowed to fall below 600 units c.c.$^{-1}$.

Step 7. Step 4 was repeated, fractions (2·5%) between 50 and 60% saturation being collected, and treated as before. Fractions with S.A. > 420 were combined. If none of the fractions was sufficiently active, steps (6) and (7) were repeated.

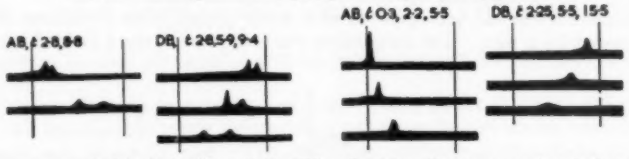
Step 8. The combined active fractions (0°) from step 7 were treated with ethanol at $-20°$ in the presence of ammonium sulphate (0·3%). Preparations with S.A. > 420 contain only two protein components (as judged by free-flow electrophoresis), and these are precipitated at widely separated ethanol–water ratios. The fraction precipitated by an equal volume of ethanol was discarded. Addition of another volume of ethanol precipitated the apoenzyme. It was

centrifuged off, dissolved in the minimum of ice-cold water, and dialysed. The final solution was clear and colourless.

Table 2 illustrates the progress of purification. Except for step 8, all the activity present in the original solution can be accounted for. Step 8 results in considerable loss of activity (*ca* 50%).

Electrophoresis.—A preparative cell of the type described by Kekwick *et al.*[9] was used in a Tiselius electrophoresis apparatus (Hilger and Watts Ltd., Model M 470). The protein solutions (final concns. 0·7—1·0%) were exhaustively dialysed (48 hr.) in Visking tubing (treated as previously described) against two changes of the appropriate buffer (1 l.). Experiments were carried out at 4°. Table 3 summarises the results obtained. The Schlieren pictures obtained with the last two preparations of Table 3 are shown in Fig. 2.

FIG. 2. *Electrophoresis in phosphate buffer* (μ 0·1, pH 6·4).



First two diagrams, material of specific activity 530. *Last two diagrams, material of specific activity* 700. AB *and* DB = *ascending and descending boundary respectively.* t = *time in hours.*

Electrophoresis in maleate buffer resulted in considerable loss of enzymic activity. This buffer, therefore, does not seem to be suitable for preparative electrophoresis of the apoenzyme. In phosphate buffer (pH 6·4) the two components (of preparations with SA > 420) are well

TABLE 2. *Purification of glutamic–aspartic transaminase.*

Step	Volume (c.c.)	Enzyme (units c.c.$^{-1}$)	Protein (mg. c.c.$^{-1}$)	Specific activity (units mg.$^{-1}$)	Purifn. factor	Yield (%)
1	64,350	34·5	9·20	3·8	[1·0]	[100]
2	14,040	158	25·80	6·1	1·6	100
3	13,140	169	9·30	18·2	4·8	100
4	630	2890	33·7	86·0	22·6	82
5	230	7080	65·5	108	28·4	73
6, 805 c.c. gel	767	1420	7·8	182	48·0	49
7, 51·5—55·5%	109	6340	30·2	210	55·5	31
6, repeat, 139 c.c. gel	211	2208	8·05	274	72·0	21
7, repeat, 51·25—57·5%	73	5958	14·19	420	110	19·5
8, 50—60% ethanol	22	6140	8·77	700	184	6

TABLE 3. *Electrophoresis of glutamic–aspartic transaminase preparations.**

S.A. prep.	Buffer	Current (mA)	No. of compts.	S.A. LC	S.A. TC
290	Barbiturate, 0·1M, pH 8·6	12	3	I	A
330	Acetate, 0·2M, pH 5·9	10	3	—	—
540	Maleate, 0·03M, pH 6·4	10	2	I	A
480	Phosphate, 0·1μ, pH 6·4	10	2	I	A
530	Phosphate, 0·1μ, pH 6·4	8	2	0	730
700	Phosphate, 0·1μ, pH 6·4	8	1	700	

* S.A. = specific activity, LC = leading component, TC = tail component, I = inactive, A = active.

separated and little loss of activity occurs. Electrophoresis in this buffer can, therefore, be used on a preparative scale as an alternative to step 8 (ethanol fractionation) of the purification given above. With a preparation of specific activity 530, fractions of the following specific activities were obtained (on successive reversal of current), LC 730, 670, 730, 690, mean 705;

[9] Kekwick, Lyttleton, Brewer, and Dreblow, *Biochem. J.*, 1951, **49**, 253.

TC 0, 77, 36, 25, mean 34. Except for the first fractions removed, some contamination of one component by the other is difficult to avoid: the figures for the tail component suggest that separation is, overall, about 95% efficient.

Properties of the Apoenzyme.—Dilute solutions (0·1%) lose activity in a few hours. Concentrated solutions (>1%) are stable for a few weeks at 0° and then slowly lose activity. Activity can be partially restored by addition of glutathione (10^{-4}M). Consistently, storage with glutathione (10^{-4}M) increases the stability. Higher concentrations appear to be inhibitory.

The effect of dialysis against chelating agents was investigated. The loss of activity (*ca.* 3%) on dialysis against EDTA (10^{-4}M) in solutions of phosphate buffer (0·1M, pH 7·4; glutathione 10^{-4}M) was the same as in an experiment without EDTA. Prolonged dialysis (48 hr., 3 changes) against a mixture of *o*-phenanthroline (10^{-3}M) and sodium salicylate (10^{-3}M) in phosphate buffer (0·1M, pH 7·4; glutathione 10^{-4}M) resulted in the same loss of activity (*ca.* 40%) as in the control experiment.

Cyanide ion, as previously reported,[10] inhibits transaminase. The following solutions were prepared and left for 60 min.: (A) pyridoxal 5′-phosphate (3×10^{-4}M), phosphate buffer (0·1M, pH 7·4), enzyme. (B) as A, plus 3×10^{-4}M-potassium cyanide added after 30 min. Assay (by method 2) of A and B, and of A to which cyanide (3×10^{-4}M) had been added immediately before assay (A′), gave the following values of v' (OD unit min.$^{-1}$), 0·219, 0·058, 0·049 for A, A′, and B respectively. The rate obtained after activation of the apoenzyme in the presence of cyanide ion is, therefore, substantially the same as when cyanide is added in the same concentration to the fully activated enzyme.

TABLE 4. *Equilibrium constant for the transamination reaction.*

Concns. (10^{-3}M) of substrates	Method 1	Method 2	Method 3	Concns. (10^{-3}M) of substrates	Method 1	Method 2	Method 3
1·25, (A, K)	—	5·9	—	1·25, (O, G)	—	5·4	—
2·5, (A, K)	—	5·7	—	5·0, (O, G)	—	6·6	5·9
5·0, (A, K)	—	6·1	6·8	10·0, (O, G)	6·8	7·9	5·4
10·0, (A, K)	6·9	7·6	6·9	20·0, (O, G)	6·5	5·1	5·7
20·0, (A, K)	7·3	7·5	6·2				

Equilibrium Constant for Transaminase.—The apparent equilibrium constant, K_e, for the reaction,

$$\underset{(G)}{\text{glutamic acid}} + \underset{(O)}{\text{oxaloacetic acid}} \rightleftharpoons \underset{(A)}{\text{aspartic acid}} + \underset{(K)}{\text{α-oxoglutaric acid}}$$

$K_e = [C_A C_K]/[C_O C_G]$, was determined at 25°, in phosphate buffer (0·1M, pH 7·38), for a highly purified enzyme preparation. Enzyme, sufficient to bring the system to chemical equilibrium within a few minutes, was added to equimolar mixtures of substrates in phosphate buffer. Analysis for oxaloacetic acid was made either by withdrawing aliquot parts and determining the absorption at 270 mμ in borate buffer at pH 9·4 (method 1), or directly in a Cary recording spectrophotometer (method 2). Appropriate controls were used in each case and all operations were conducted sufficiently quickly for corrections required for decomposition of oxaloacetic acid to be very small. Glutamic acid was estimated manometrically as described above (method 3). The results are shown in Table 4. The mean value of K_e was 6·5 (at 25°).

DISCUSSION

It has been established that the assay methods correctly measure the initial rate of the enzyme-catalysed reaction between L-aspartate and α-oxoglutaric acid. At high enzyme concentrations, method (2) (in which a direct-recording spectrophotometer is used) must be employed. A similar technique has been described by Cammarata and Cohen [4] and by Sizer and his co-workers.[6] The latter express their results in terms of a pseudo-rate coefficient derived by assuming the reaction to be a reversible first-order process. However, such a procedure is arbitrary * and appears to have no advantage, especially since v'

* One advantage claimed is that no use is made of the value of the extinction coefficient of oxaloacetic acid (ε). However, to find v (the initial reaction rate expressed in mole l.$^{-1}$ time^{-1}) from any set of data obtained by measuring optical density changes, the appropriate value of ε must be used.

[10] Bonavita and Scardi, *Experientia*, 1958, **14**, 7.

(the initial reaction rate expressed in O.D. unit time^{-1}) can easily be found as described above.

The holoenzyme has been resolved by heating it at pH 6·0. All the activity originally present can be restored by addition of pyridoxal 5′-phosphate or by pyridoxamine 5′-phosphate. The suggestion by Cammarata and Cohen [4] that resolution results in some irreversible loss of activity is therefore unfounded.

Except in the final (ethanol) fractionation, no loss of total activity occurs in any step of the purification procedure (*i.e.*, the total activity present in the fraction selected for the next stage and in the discarded fractions is equal to the activity before fractionation). Electrophoresis (phosphate buffer, pH 6·4) shows that, after step 7, the preparation contains two proteins. Electrophoretic separation gives the apoenzyme with a specific activity of *ca.* 700 units mg.$^{-1}$. No loss of total activity occurs during this process. Ethanol fractionation also separates the two proteins; precipitation occurs at two well-separated, well-defined ethanol–water ratios. The specific activity of the apoenzyme obtained in this way is also *ca.* 700 units mg.$^{-1}$, and the preparation is homogeneous with respect to electrophoresis in phosphate buffer at pH 6·4 (Fig. 2). Therefore, although considerable loss of total activity (*ca.* 50%) occurs in ethanol fractionation, the apoenzyme obtained is not, apparently, contaminated with inactivated enzyme.

Some previous workers [4] have reported that electrophoresis of impure glutamic–aspartic transaminase in phosphate buffer showed the presence of two components with transaminase activity. However, no experimental details of how this was established were given. Our experience is not consistent with this. Electrophoresis of any preparation with a specific activity greater than *ca.* 420 units mg.$^{-1}$, either in phosphate or in maleate buffer, showed only two components, of which one was active and the other inactive. Our results do not indicate, therefore, any abnormal behaviour of the apoenzyme in phosphate buffer.

It is important to compare the maximum value of the specific activity obtained by us with the values reported by other workers. Detailed comparison is, however, difficult since, with this enzyme, the reaction rate varies in a complicated way with enzyme, substrate, and hydrogen-ion concentration, and also depends on the nature of the buffer used. Our best preparation (specific activity *ca.* 700 units mg.$^{-1}$) gives an initial reaction rate (R), under the stated standard conditions, of $97{\cdot}2 \times 10^{-6}$ mole per min. per mg. of protein (at 25°). For the first four preparations reported (refs. 1—4), the corresponding figures are, for our conditions, *ca.* 5, 8, 10, and 12×10^{-6} respectively. The comparison is not very precise, since different substrate concentrations were used. However, the figures show that these preparations contained much inactive protein and this is consistent with the low purification factors reported (*ca.* 11, 17, 26, 14, respectively, compared with 184 for the present work), and with the observed electrophoretic behaviour. From the data given by Lis [5] it can be calculated that her homogeneous preparation of the holoenzyme would give, under our conditions, an initial reaction rate (R) in the range $25—35 \times 10^{-6}$ mole min.$^{-1}$ mg.$^{-1}$. It may be, therefore, that her preparation suffered some irreversible inactivation during purification.

Comparison with the data of Sizer *et al.*[6] is harder since the standard conditions used by these workers differ in temperature, pH, and buffer from ours. Our preparation gives, at 37° and under our assay conditions, a value $R = 181 \times 10^{-6}$ mole min.$^{-1}$ mg.$^{-1}$. Calculation shows that the preparation of Sizer *et al.*, under the conditions described by them, gave $R = 158 \times 10^{-6}$ moles min.$^{-1}$ mg.$^{-1}$ (at 37°; ε_{280} oxaloacetic acid = 630 in tris-buffer of pH 8·4). We have tried to make a better comparison by measuring reaction rates with the same enzyme sample under both conditions of reaction. The results indicate that the specific activity of our sample is slightly greater.* This is consistent

* Some ambiguity remains, however, since, in our hands, for reactions in this buffer, the results obtained by using the direct spectrophotometric method (method 2) are different from those obtained when aliquot parts are diluted with borate buffer (method 1).

with the report of Sizer *et al.* that their preparation contained *ca.* 13% of inactive protein.

Concentrated solutions of the apoenzyme are stable at 0° for some weeks in the presence of glutathione. The stabilising effect of this compound may be due to its ability to preserve thiol groups in the reduced form, although transaminase does not appear to contain a catalytically functional thiol group.[11]

No evidence has been found for the involvement of a metal cation in the catalytic activity of the enzyme. Dialysis against buffered solutions of EDTA, or of *o*-phenanthroline (effective chelating agent for Fe^{2+}) and sodium salicylate (effective for Fe^{3+}), gave no greater loss of activity than dialysis against buffer alone. This is consistent with the results of other workers: apart from some experiments on a transaminase of plant origin,[12] attempts to show that enzymic transamination involves a catalytically functional metal cation have yielded negative results.

Contrary to the claim of Bonavita and Scardi [10] the formation of the holoenzyme is not impeded by the presence of cyanide ions. No evidence is produced from experiments concerned with inhibition by cyanide ions that pyridoxal 5′-phosphate is attached to the protein through the aldehyde group.

The mean value of the equilibrium constant ($K_e = 6{\cdot}5$, at 25°) for the overall reaction obtained with a highly purified enzyme sample is in excellent agreement with the mean value ($K_e = 6{\cdot}75$) found by Krebs [13] using a crude preparation from horse heart. Braunstein's suggestion [11] that the position of equilibrium depends on the purity of the enzyme sample used appears, therefore, to be unfounded.

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[11] Braunstein, *Adv. Protein Chem.*, 1947, **3**, 1.
[12] Patwardhan, *Nature*, 1958, **181**, 187.
[13] Krebs, *Biochem. J.*, 1953, **54**, 82.

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332. *The Nitrous Acid–Tributyl Phosphate Complex.*

By J. M. Fletcher, D. Scargill, and J. L. Woodhead.

Tributyl phosphate extracts nitrous acid almost quantitatively from aqueous solutions. The spectrum, from 320 to 400 mμ, shows the enhanced fine structure characteristic of molecular nitrous acid and of alkyl nitrites. Distribution data indicate a 1 : 1 complex, [Bu_3PO_4,HO·NO], and infrared spectra that the hydrogen-bonding to the phosphoryl-oxygen atom modifies the bonding in nitrous acid towards an ionic structure.

It is known, from work on tributyl phosphate as a solvent for the extraction of metal nitrates from aqueous nitric acid, that nitrous acid formed in the system by thermal or radiolytic reactions is largely taken up by the organic phase. We have now been able to establish the nature of the complex responsible for the abnormally high distribution coefficient (q) of nitrous acid (compared with the coefficients of other acids). The stability of the complex is so great that, even in the presence of traces of water, solutions of up to M-nitrous acid may be prepared in tributyl phosphate.

The ultraviolet spectra of these solutions of nitrous acid in water-saturated tributyl phosphate show five sharp bands (Table 1) between 320 and 400 mμ. These can be

attributed to molecular nitrous acid, since similar though weaker bands occur in the spectra of nitrous acid both as vapour [1] and when dissolved [2] in concentrated sulphuric, perchloric, and phosphoric acid. As Beer's law is obeyed (from 10^{-2} to 5×10^{-4}M-acid) it is concluded that the nitrous acid is present entirely in the molecular form.

TABLE 1. *Absorption spectra of nitrous acid in 100% tributyl phosphate.*

$\lambda_{max.}$ (mμ)	339		349·75		361·5		375·5		391
$\Delta\nu_{max.}$ (cm.$^{-1}$)		910		930		1030		1050	
$\lambda_{min.}$ (mμ)		343·5		355		368		382·5	
ε	29	18·5	54	22·5	83	23·5	96	16·5	57

TABLE 2. *Changes in $q(HNO_2)$ with tributyl phosphate concentration.*

Total HNO_2 = 0·0125M; $HClO_4$ org., *ca.* 10^{-3}M.

Bu_3PO_4 (M)	0·025	0·05	0·075	0·10	0·15
$q(HNO_2)$ (org./aq.)	0·23	0·5	0·8	1·2	2·1

TABLE 3. *Infrared spectra of nitrous acid and methyl nitrite (in cm.$^{-1}$).*

HNO_2 in 100% Bu_3PO_4	HNO_2 in 10—20% Bu_3PO_4	HNO_2 vapour [a]	MeO·NO vapour [b]	Assignment	HNO_2 in 100% Bu_3PO_4	HNO_2 in 10—20% Bu_3PO_4	HNO_2 vapour [a]	MeO·NO vapour [b]	Assignment
3055	3065	3590		*trans* } O–H	1402	1391	1292		*cis* } O–H
2733	2736	3426		*cis* } stretch	—[c]	1306	1260		*trans* } bend
1629	1633	1696	1681	*trans* } N=O	926	941	856	844	*cis* } N–O
—[c]	1591	—[d]	1625	*cis* } stretch	881	872	794	814	*trans* } stretch

[a] Jones, Badger, and Moore, *J. Chem. Phys.*, 1951, **12**, 1599. Tarte, *ibid.*, 1952, **20**, 1570. [c] Obscured by Bu_3PO_4. [d] Obscured by NO_2.

The slope of the curve obtained when log q, for traces of nitrates, is plotted against log $[Bu_3PO_4]$ has been used,[3] for up to 5% (0·18M) tributyl phosphate in inert diluents, to determine the composition of the complex in the organic phase. The limiting slope of the corresponding curve for $q(HNO_2)$ (Table 2) indicates that one molecule of tributyl phosphate is associated with one of nitrous acid and suggests that the complex has the composition Bu_3PO_4,HNO_2. The absence of significant absorption bands of water in the infrared spectra of 10—20% solutions of the phosphate, both with and without nitrous acid, shows that the complex does not contain water.

The complex shows a duplication (Table 3) of the infrared absorption bands of nitrous acid which can be attributed to *cis*- and *trans*-rotational isomers as in nitrous acid vapour [4] and alkyl nitrites.[5] In all three cases the bands of the *trans*-isomers are the more intense. The infrared frequencies (Table 3) of the N=O bands are substantially lower, and those of the N–O bands substantially higher, for Bu_3PO_4,HNO_2 than for nitrous acid vapour and methyl nitrite. This indicates a trend towards equivalence of the two nitrogen–oxygen bonds such as occurs in nitritometal complexes where these frequencies become [6] 1460 and 1065 cm.$^{-1}$ respectively. Associated changes (Table 3) in the O–H frequencies from those in nitrous acid vapour, and in the P=O frequency (Table 4) from that in tributyl phosphate show that this modification in the nitrite group arises from hydrogen-bonding with the electronegative phosphoryl-oxygen atom ($\equiv P\rightarrow \overset{\delta-}{O}\cdots \overset{\delta+}{H}\rightarrow \overset{\delta-}{O}=N=O$). The strength of the hydrogen-bonding in the complex is intermediate (Table 4) between that for water and for nitric acid in the phosphate; the shifts in ν_{OH} due to hydrogen-bonding ($\Delta\nu_{OH}$) from the values in the vapour state are regarded as a measure of the strength of the hydrogen bond and are proportional (Table 4) to the shifts in ν_{PO} ($\Delta\nu_{PO}$).

[1] Porter, *J. Chem. Phys.*, 1951, **19**, 1278.
[2] Bayliss and Watts, *Austral. J. Chem.*, 1956, **9**, 319.
[3] Hesford and McKay, *Trans. Faraday Soc.*, 1958, **54**, 573.
[4] Jones, Badger, and Moore, *J. Chem. Phys.*, 1951, **19**, 1599.
[5] Tarte, *J. Chem. Phys.*, 1952, **20**, 1570.
[6] Penland, Lane, and Quagliano, *J. Amer. Chem. Soc.*, 1956, **78**, 887.

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The frequency interval (Table 1) between the maxima of the ultraviolet absorption bands of the complex increases with increase in wavelength, as with the alkyl nitrites,[5] the average separation being 980 cm.$^{-1}$. For the alkyl nitrites [5] this frequency interval has been attributed to a vibrational transition of the excited state of the nitrite group as a

TABLE 4. *Variation of hydrogen bonding with ν_{PO} in tributyl phosphate complexes.*

	ν_{OH} for vapour	ν_{OH} for complex	ν_{PO} for complex	$\Delta\nu_{OH}/\Delta\nu_{PO}$ [a]
H_2O	3676 [b]	3450	1264	11·9
trans-HNO_2	3590 [c]	3060	1238	11·8
cis-HNO_2	3426 [c]	2735	1226	12·1
HNO_3	3560 [d]	2611 [e]	1208 [e]	12·6

[a] $\Delta\nu_{OH}$ is the difference between the value for the vapour and that when hydrogen-bonded to PO; $\Delta\nu_{PO}$ is the difference from that in tributyl phosphate (1283 cm.$^{-1}$). [b] Average of asymmetric and symmetric stretching frequencies for H_2O monomer; Thiel, Becker, and Pimentel, *J. Chem. Phys.*, 1957, **27**, 486. [c] Ref. 4. [d] Cohn, Ingold, and Poole, *J.*, 1952, 4272. [e] Nukada, Naito, and Maeda, *Bull. Chem. Soc. Japan*, 1960, **33**, 894.

whole, tending towards the structure O=N=O with fractional valencies. The prominence of the ultraviolet bands in Bu_3PO_4,HNO_2 supports this hypothesis since the hydrogen-bonding to P=O is able to modify the HNO_2 molecule towards H···O=N=O. The ultraviolet absorption bands of the complex show evidence for slight asymmetry due, as for the alkyl nitrites, to superimposition of two band systems, namely, those for the *cis*- and the *trans*-isomer.

The intensity of the ultraviolet bands, together with an almost quantitative extraction of nitrous acid by 100% tributyl phosphate, provides a sensitive method for the estimation [7] of aqueous nitrous acid at concentrations down to 10^{-4}M. Such determinations may require adjustment of the aqueous solutions to suitably dilute acid conditions, since (i) values of $q(HNO_2)$ fall in the presence of high concentrations of other acids which are extracted by the phosphates, *e.g.*, for 100% tributyl phosphate, from ~100 for $[HClO_4]_{org.}$ <0·1M to 25 for $[HClO_4]_{org.}$ = 1·2M, and (ii) there is appreciable quenching of the ultraviolet absorption bands with high concentrations (>0·5M) of other acids in the organic phase.

The high extraction, by organic solvents containing donor oxygen groups, of nitrous acid, compared with that of other mineral acids [for 100% Bu_3PO_4 with <0·5M-acid in the aqueous phase; cf. $q(HNO_2)$ ~100, with [8] $q(HF) = q(HClO_4) \sim 1$, $q(HNO_3) = q(HCl) = q(H_2SO_4)$ ~0·01] is largely a reflection of the ionisation of the other acids in the aqueous phase. Thus the value of the distribution coefficient for undissociated nitric acid, calculated after allowing for ionisation in the aqueous phase, is about 50 (for our conditions). For hydrofluoric acid, the relatively low value of q is attributed to stronger hydrogen-bonding in the aqueous phase.

EXPERIMENTAL

Solutions of nitrous acid in tributyl phosphate or tributyl phosphate–kerosene were prepared and examined at room temperature (~22°) by equilibration of the solvent with aqueous phases containing sodium nitrite in 10^{-2}M-sodium hydroxide to which perchloric or hydrochloric acid was added. Concentrated (0·5—1·0M) solutions for infrared examination were prepared by equilibration at 0°. Equilibrium between the phases was attained in less than 1 min.

Nitrous acid in the organic phases was determined by measuring the extinction coefficient at 391 mμ (Table 1).

Ultraviolet spectrophotometric measurements were made at room temperature with a Unicam S.P. 500 spectrophotometer, and infrared measurements at room temperature with a Hilger H-800 double-beam spectrometer equipped with a rock-salt prism. Samples for infrared examination were mounted as thin films ($\leqslant 2{\cdot}5 \times 10^{-3}$ cm.) between silver chloride windows.

The authors thank Mr. A. M. Deane for his advice during the infrared measurements.

CHEMISTRY DIVISION, A.E.R.E., HARWELL. [*Received, October 28th*, 1960.]

[7] Woodhead, U.K.A.E.A. Document A.E.R.E., R-3432, 1960.
[8] Hesford and McKay, *J. Inorg. Nuclear Chem.*, 1960, **13**, 156.

333. *The Mechanism of Epoxide Reactions. Part III.*[1] *The Reactions of* p-*Bromo-*(1,2-*epoxyethyl*)*benzene and* p-(1,2-*Epoxyethyl*)*toluene with Benzylamine.*

By J. K. Addy, R. M. Laird, and R. E. Parker.

Rate constants at three temperatures have been determined for the first reactions of *p*-bromo-(1,2-epoxyethyl)benzene and *p*-(1,2-epoxyethyl)toluene with benzylamine. Product analyses have been carried out by infrared spectroscopy and the results have been used to separate the measured rate constants into rate constants for normal and for abnormal attack. It appears from these preliminary results that the effect of substituents is such that the normal reaction (attack at CH_2) has a positive value for the Hammett reaction constant, ρ, while the abnormal reaction (attack at CH) has a negative ρ.

Of the epoxide–amine reactions reported in Parts I [2] and II,[1] the only one to give significant amounts of both normal and abnormal product was that between 1′,2′-epoxyethylbenzene and benzylamine. This reaction was accordingly chosen as the starting point for an investigation into the effect of substituents on the rates of both normal and abnormal attack on an unsymmetrical epoxide, and the present paper records the results of a kinetic study of the reactions between benzylamine and the *p*-bromo- and *p*-methyl derivatives of 1′,2′-epoxyethylbenzene. The bromo- and methyl groups may be taken as unambiguous examples of electron-withdrawing and electron-releasing groups, respectively, and, since they are in the *para*-position, the electronic effects should be uncomplicated by any steric effect.

Fuchs and VanderWerf [3] have shown that, in reaction with lithium borohydride, *p*-bromo-(1,2-epoxyethyl)benzene gives a higher proportion of normal product (84%), and *p*-(1,2-epoxyethyl)toluene a lower proportion (32%), than does 1′,2′-epoxyethylbenzene (74%). No kinetic measurements were carried out, however, and the change in proportion of normal product could be due to a change in the rate of normal attack, or to a change in the rate of abnormal attack, or both. Fuchs [4] also studied the kinetics of the reactions of the same three epoxides with sodium thiosulphate in aqueous ethanol at 25° and found higher rates of reaction for *p*-bromo-(1,2-epoxyethyl)benzene ($k = 3{\cdot}07 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$) and *p*-(1,2-epoxyethyl)toluene ($k = 2{\cdot}40 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$) than for 1′,2′-epoxyethylbenzene ($k = 2{\cdot}04 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$). However, no product analyses were carried out and it is not possible, therefore, to divide the overall rate constants into rate constants for normal attack and for abnormal attack.

The only other quantitative comparison of the three epoxides is the determination by Park and Fuchs [5] of the product ratios for the hydrogenations in the presence of platinum oxide in ethanol. Here the direction of change [100% abnormal product from 1′,2′-epoxyethylbenzene and *p*-(1,2-epoxyethyl)toluene, 82% from *p*-bromo-(1,2-epoxyethyl)benzene] is the same as in the reactions with lithium borohydride. However, the hydrogenations are heterogeneous reactions and almost certainly do not involve the simple attack of a nucleophile at an epoxide carbon atom and they are, consequently, not comparable to the reactions with lithium borohydride, sodium thiosulphate, or benzylamine.

In Part II [1] the reaction between benzylamine and 1′,2′-epoxyethylbenzene was followed by independent determinations of primary amine and of tertiary amine and the analytical figures were used to calculate rate constants both for the first reaction and for the second reaction (*i.e.*, reaction between the epoxide and the product of the first

[1] Part II, Isaacs and Parker, *J.*, 1960, 3497.
[2] Part I, Chapman, Isaacs, and Parker, *J.*, 1959, 1925.
[3] (*a*) Fuchs and VanderWerf, *J. Amer. Chem. Soc.*, 1954, **76**, 1631; (*b*) Fuchs, *ibid.*, 1956, **78**, 5612.
[4] Fuchs, *J. Org. Chem.*, 1958, **23**, 902.
[5] Park and Fuchs, *J. Org. Chem.*, 1957, **22**, 93.

reaction). In the present work a four-fold excess of benzylamine was used and the second reaction was thereby suppressed to such an extent that it was insignificant for at least the first 50% of the first reaction. Under these conditions it is possible to follow the first reaction for the first 50% of its course by determinations of primary amine alone.

Product analyses were carried out as before,[2] by comparing the infrared spectrum of the reaction product with that of the normal isomer and of the abnormal isomer. It was also shown that, for *p*-bromo-(1,2-epoxyethyl)benzene at 49°, the same product ratio was obtained from a reaction with an eight-fold excess of benzylamine over epoxide as from one with a four-fold excess. It follows from this that the normal and the abnormal reaction must have the same kinetic order and that, since the overall reaction obeys the second-order rate law, they must both in fact be of second order.

Table 1 lists the measured fractions of normal and abnormal isomer and the rate constants for normal (k_N) and abnormal (k_A) attack. The Arrhenius parameters and the rate constants interpolated to 49° are collected in Table 2. It is clear from Table 2 that the rate of attack at the normal position is increased by the electron-withdrawing *p*-bromo-group and decreased by the electron-releasing *p*-methyl group. The normal reaction therefore has a positive value of the Hammett reaction constant, ρ (although the number

TABLE 1. *Isomer proportions and measured rate constants,* 10^5k (l. mole^{-1} sec.$^{-1}$).

	Temp.	Normal	Abnormal	k_N	k_A
1′,2′-Epoxyethylbenzene [1]	20·00°	0·83	0·17	1·15	0·24
	40·50	0·78	0·22	4·99	1·41
	59·68	0·73	0·27	18·5	6·8
p-Bromo-(1,2-epoxyethyl)benzene	20·10	0·85	0·15	2·20	0·39
	35·30	0·82	0·18	5·29	1·16
	49·20	0·79	0·21	11·6	3·1
p-(1,2-Epoxyethyl)toluene	25·85	0·45	0·55	0·99	1·21
	35·20	0·45	0·55	2·01	2·46
	49·00	0·45	0·55	5·2	6·3

TABLE 2. *Rate constants interpolated to* 49°, *and Arrhenius parameters.* (*k and A in* l. mole^{-1} sec.$^{-1}$; *E in* kcal. mole^{-1}.)

	Normal reaction			Abnormal reaction		
	10^5k_N	E	log A	10^5k_A	E	log A
1′,2′-Epoxyethylbenzene [1]	9·3	13·5	5·1	3·0	16·2	6·5
p-Bromo-(1,2-epoxyethyl)benzene	11·3	10·7	3·3	3·0	13·4	4·6
p-(1,2-Epoxyethyl)toluene	5·2	13·7	5·0	6·3	13·7	5·1

These values of E and log A for the abnormal reaction of 1′,2′-epoxyethylbenzene are different from those given in Part II.[1] The latter are incorrect and arose because of an unfortunate transposition of 16·24 kcal. to 14·26 kcal., and the use of this incorrect value in the calculation of log A.

of substituents studied is insufficient to justify an attempt to evaluate ρ). The effect of substituents on the rate of attack at the abnormal position is less clear. While the electron-releasing *p*-methyl group undoubtedly increases the abnormal rate, the effect of the *p*-bromo-group is small and the direction of the effect depends on the choice of temperature for comparison of the abnormal rate constants of 1′,2′-epoxyethylbenzene and *p*-bromo-(1,2-epoxyethyl)benzene. The last two rate constants, since they constitute only about 20% of the total measured rate constants in each case, are subject to greater uncertainty than the others. In spite of this, it seems very likely that the abnormal reaction has a negative value for ρ.

This effect of a given substituent of increasing the reactivity at one position and decreasing it at another within the same molecule is believed to be unique. It is easy to understand why the abnormal reaction should have a negative ρ, for the opening of the highly strained three-membered ring should not require very much help from the reagent and would be expected to take place by a mechanism in which bond-breaking is more important

than bond-making.[6] Such mechanisms, of course, result in a negative ρ. It is not immediately obvious why the normal reaction does not also have a negative ρ, since the same considerations of ring-strain apply. However, as has been pointed out in Part I,[2] the reaction at the normal position of an unsymmetrical epoxide is an unusual type of bimolecular substitution in which the substituent group is almost exactly equidistant from both ends of the breaking bond. Thus, even though bond-breaking may still be the dominant factor, the effect of a substituent on the bond-breaking energy will be small or non-existent. The remaining effect of the substituent, that on the bond-making energy (*i.e.*, the repulsion energy), will then be dominant and this will give rise to a positive ρ.

This work is being extended to include *meta*- and other *para*-substituted 1′,2′-epoxyethylbenzenes, and the results so far obtained support the above interpretation.

Experimental

Materials.—*p*-Bromo-(1,2-epoxyethyl)benzene, prepared by Fuchs and VanderWerf's method,[3a] had m. p. 26—27°, b. p. 91—93°/2 mm. *n*-(1,2-Epoxyethyl)toluene, prepared by Fuchs's method,[3b] had b. p. 51—52°/0·1 mm., n_D^{26} 1·5277. Benzylamine was purified as in Part II.[1] Ethanol was dried and adjusted to 99·80% w/w as in Part I.[2]

Rate Measurements.—The reactions were carried out in the same way as those in Part I,[2] but with an initial concentration of epoxide of *ca.* 0·1M and of amine of *ca.* 0·5M. They were followed by determinations of benzylamine alone and these were carried out as in Part II,[1] except that the aliquot parts (1 ml.) were added to 20 ml. of 1% ethanolic salicylaldehyde and the resulting solutions were set aside for at least 12 hr. before being made up to 100 ml.

Synthesis of Products.—*2-Benzylamino*-1-p-*bromophenylethanol* *p*-Bromo-(1,2-epoxyethyl)-benzene (3 g., 0·015 mole) was added to benzylamine (7·7 g., 0·075 mole) in absolute ethanol (15 ml.) and the solution was kept at 50° for 3 days. Removal of ethanol and excess of benzylamine at 100°/15 mm., followed by crystallisation of the residue from ethanol, gave *2-benzylamino*-1-p-*bromophenylethanol*, m. p. 109·5° (Found: C, 59·6; H, 5·4; N, 4·7. $C_{15}H_{16}BrNO$ requires C, 58·9; H, 5·3; N, 4·6%).

2-Benzylamino-2-p-*bromophenylethanol.*—4-Bromobenzyl bromide was prepared from *p*-bromotoluene by Weizmann and Patai's method [7] and the crude product (m. p. 61—62°) was converted into 4-bromobenzyl cyanide according to Adams and Thal's method [8] for benzyl cyanide. Hydrolysis of the cyanide by Misra and Shukla's method,[9] followed by crystallisation of the product from water, gave *p*-bromophenylacetic acid, m. p. 114° (lit.,[9] 114°). Treatment of this acid according to Hahn and Walter's method [10] for phenylacetic acid gave *ethyl α-bromo*-p-*bromophenylacetate*, b. p. 132—133°/1 mm. (Found: C, 37·4; H, 3·2; Br, 49·9. $C_{10}H_{10}Br_2O_2$ requires C, 37·3; H, 3·1; Br, 49·6%).

The bromo-ester (20 g., 0·06 mole) in dry ether was added to an excess of benzylamine (20 g., 0·19 mole), and the mixture was kept at 25° for 18 hr. and filtered from precipitated benzylamine hydrobromide. Removal of the ether and distillation *in vacuo* of the residue gave *ethyl α-benzylamino*-p-*bromophenylacetate*, b. p. 180°/0·01 mm. (Found: C, 58·7; H, 5·3; N, 4·0; Br, 22·6. $C_{17}H_{18}BrNO_2$ requires C, 58·6; H, 5·2; N, 4·0; Br, 23·0%). The amino-ester (8 g., 0·023 mole) in dry ether was added dropwise to a slurry of lithium aluminium hydride (1 g., 0·026 mole) in boiling ether (100 ml.). The mixture was heated under reflux for a further 2 hr., after which water was added. After filtration, the ethereal layer was separated, dried (Na_2SO_4), and evaporated. Crystallisation of the residue from light petroleum (b. p. 60—80°) gave *2-benzylamino*-2-p-*bromophenylethanol*, m. p. 63° (Found: C, 59·5; H, 5·2; N, 4·5. $C_{15}H_{16}BrNO$ requires C, 58·9; H, 5·3; N, 4·6%).

2-Benzylamino-1-p-*tolylethanol.*—4-Methylphenacyl bromide, prepared by Bose's method,[11] was allowed to react with benzylamine (2 mol.) in dioxan at 60° for 5 min. The theoretical amount of benzylamine hydrobromide was filtered off and the solution of the unstable amino-ketone was reduced with aqueous sodium borohydride. Working up in the usual way and

[6] Parker and Isaacs, *Chem. Rev.*, 1959, **59**, 737.
[7] Weizmann and Patai, *J. Amer. Chem. Soc.*, 1946, **68**, 150.
[8] Adams and Thal, *Org. Synth.*, 1922, **2**, 9.
[9] Misra and Shukla, *J. Indian Chem. Soc.*, 1951, **28**, 480.
[10] Hahn and Walter, *Annalen*, 1907, **354**, 127.
[11] Bose, *J. Indian Chem. Soc.*, 1926, **3**, 205.

crystallisation from ethanol gave *2-benzylamino*-1-p-*tolylethanol*, m. p. 119—120° (Found: C, 79·9; H, 8·0; N, 5·6. $C_{16}H_{19}NO$ requires C, 79·9; H, 7·9; N, 5·8%). Identical material was obtained from the reaction of *p*-(1,2-epoxyethyl)toluene with benzylamine in ethanol, by crystallisation of the crude product from ethanol.

2-Benzylamino-2-p-*tolylethanol*.—Methyl α-chloro-*p*-tolylacetate was prepared by Baker, Ollis, and Poole's method [12] and, after careful purification, had b. p. 100—118°/0·6—1 mm., n_D^{19} 1·524. In view of the boiling range the material was submitted to gas chromatography on a column of Silicone resin supported on Celite and was thereby shown to be homogeneous (Found: C, 60·3; H, 5·6; Cl, 18·0. Calc. for $C_{10}H_{11}ClO_2$: C, 60·4; H, 5·6; Cl, 17·9%). Reaction with benzylamine (2 mol.) in di-isopropyl ether at 60° for 20 hr. gave a theoretical amount of benzylamine hydrochloride which was removed by filtration. After several unsuccessful attempts to isolate methyl α-benzylamino-*p*-tolylacetate by distillation, the solution of amino-ester was reduced directly with an excess of lithium aluminium hydride. Working up in the usual way gave *2-benzylamino*-2-p-*tolylethanol*, b. p. 120°/3 × 10^{-4} mm., n_D^{24} 1·5675 (Found: C, 81·4; H, 8·0; N, 6·2. $C_{16}H_{19}NO$ requires C, 79·9; H, 7·9; N, 5·8%). A further quantity of this material was isolated from the reaction of *p*-(1,2-epoxyethyl)toluene with benzylamine in ethanol, by working-up of the mother-liquor remaining after crystallisation of 2-benzylamino-1-*p*-tolylethanol. The liquid product solidified on long storage and, after crystallisation from light petroleum (b. p. 40—60°), had m. p. 72—73° (Found: C, 80·0; H, 7·9; N, 5·7%). The two preparations had identical infrared spectra.

Product Analysis.—Infrared analysis. Infrared spectra were determined for (*a*) the actual reaction product (obtained by allowing the reaction in ethanol to go to completion and distilling the product *in vacuo* in such a way as to obtain the total secondary amine fraction free from other compounds), (*b*) the normal product, (*c*) the abnormal product, and (*d*) various synthetic mixtures of the normal and abnormal product. All the measurements were made on chloroform solutions with a Unicam S.P. 100 double-beam, infrared spectrophotometer.

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THE UNIVERSITY, SOUTHAMPTON. [*Received, November 15th,* 1960.]

[12] Baker, Ollis, and Poole, *J.*, 1950, 1548.

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334. *Antimony Halides as Solvents. Part II.*[1] *Conductance Data on Solutions of Organic Chlorides in Antimony Trichloride at 75°.*

By ANTHONY G. DAVIES and E. C. BAUGHAN.

Conductance data are presented for tetramethylammonium and triphenylmethyl chloride which are 1-1 strong electrolytes; application of Walden's rule confirms the earlier evidence for abnormal mobility of chloride ion.

Data are also presented for bornyl, n-decyl, 1-ethylcyclohexyl, cyclohexyl, diphenylmethyl, cinnamyl, and benzyl chloride. These are shown to ionise principally in the new mode $2RCl \rightleftharpoons R_2Cl^+ + Cl^-$, though in dilute solution the simple mode $RCl \rightleftharpoons R^+ + Cl^-$ can be detected. Values for these equilibrium constants are worked out and discussed.

PART I of this series [1] gives data on freezing-point depressions in antimony trichloride. Hydrocarbons show a normal depression, except for stilbene which dimerises. The simple salts potassium chloride, cæsium chloride, and tetramethylammonium chloride give two ions each per molecule and the ionic-strength effects are explicable by Debye-Hückel theory.

Triphenylmethyl chloride also was shown to be a 1-1 strong electrolyte in antimony trichloride, as opposed to other solvents where it is only slightly ionised. The present

[1] Part I, Porter and Baughan, *J.*, 1958, 744.

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work is concerned with the electrical conductance of tetramethylammonium and triphenylmethyl chloride, confirming the freezing-point data, and with the electrical conductance of several aliphatic and phenyl-substituted aliphatic chlorides.

The most precise previous conductance data [2] on antimony trichloride solutions of inorganic chlorides refer to 99°; we have, however, preferred to work at 75° since this is only just above the freezing point (73·17°) so that our activity data [1] can be used without significant corrections, and since the lower temperature diminishes the difficulties caused by solute volatility and the risk of side-reactions. During this work three papers appeared on conductance in antimony trichloride (at 99° mainly) by Jander and Swart; [3] these were more concerned with inorganic solutes, but confirm our work at several points, in particular for triphenylmethyl chloride.

Experimental

Materials.—" AnalaR " antimony trichloride was further purified by repeated distillation under reduced pressure in an atmosphere of dry, oxygen-free nitrogen. The final distillation into the conductivity cell was carried out over highly pure antimony (99·999%) to reduce any remaining antimony pentachloride to the trichloride. Qualitative tests, based on the intense colour given with triphenylamine with antimony pentachloride,[4] showed the latter to be absent from the purified antimony trichloride.

Diphenylmethyl, cinnamyl, benzyl, cyclohexyl, n-decyl, and bornyl chloride were commercial specimens, 1-ethylcyclohexyl chloride was prepared from cyclohexanone, and triphenylmethyl chloride from triphenylmethanol. Triphenylmethyl chloride and bornyl chloride were repeatedly recrystallised, and the latter finally sublimed at 30 mm. The liquid chlorides were, after preliminary drying, fractionated through a Widmer (spiral band) column until constant refractive index was obtained. The physical properties of the samples used were as tabulated. No attempt was made to separate isomers of cinnamyl chloride.

Chloride	B. p./mm.	n_D	Chloride	B. p./mm.	n_D
Triphenylmethyl	(113·5—115·5°) *	—	Benzyl	78°/21	1·5383/20·5°
Bornyl	(131°) *	—	Cyclohexyl	142°/760	1·4609/22·5°
Diphenylmethyl	107°/0·1	1·5950/22·5°	1-Ethylcyclohexyl	83—86°/23	1·4620/22·5°
Cinnamyl	68—71°/0·5	1·5780/26°	n-Decyl	111—112°/19	1·4367/22·5°

* M. p.

Apparatus.—The conductivity-cell resistance was measured at 1000 c.p.s. by a conventional a.c. bridge with grounding system using audio null-point detection *via* an amplifier.

The conductivity cells were made of Pyrex glass with bright platinum electrodes and were of a conventional type modified for work with small volumes. Since antimony trichloride expands on freezing with force enough to break the glass electrode holders (cf. also Klemensiewicz *et al.*[2]), the cells were made in a λ-shape with both cylindrical arms slightly tapered. Solutions were made and cooled in the main arm; the side arm contained the electrodes; the solutions could be well mixed by pouring from arm to arm. The main arm carried a ground-on cell cap designed for simultaneous passage of dry nitrogen, while the solute entered through a smaller cap; the cell-cap could be kept warm to avoid condensation, and all joints were ground externally and lubricated by Teflon sleeves. Measurements were made in a paraffin thermostat bath at 75° in subdued light (some of the deeply coloured solutions appeared to be photosensitive); cell-constants were determined [5] by using potassium chloride solutions in de-ionised water at 25°.

Procedure.—About 25 c.c. of purified solvent were distilled under reduced pressure of dry nitrogen directly into the cell, a small fore-run being rejected. The entire still, when cool, was transferred to a dry-box where, in dry nitrogen, the cell was removed and closed with a ground-on cap. The liquid was then degassed by lowering the pressure, which reduced the specific conductance κ_0 to 4—6 × 10^{-6} ohm^{-1} $cm.^{-1}$; this increased only very slowly when the liquid was kept in the cell at 75°. After degassing, the amount of solvent was found by direct weighing;

[2] Klemensiewicz and Balówna, *Roczniki Chem.*, 1930, **10**, 481; 1931, **11**, 683.
[3] Jander and Swart, *Z. anorg. Chem.*, 1959, **299**, 252; **301**, 54, 80.
[4] Taylor and Baker, " Sidgwick's Organic Chemistry of Nitrogen," Oxford Univ. Press, 1937, p. 63.
[5] Lind, Zwolenik, and Fuoss, *J. Amer. Chem. Soc.*, 1959, **81**, 1557.

the cell-cap was fitted in the dry-box, and the whole cell placed in the thermostat. Solutes were added to the cell at time intervals depending on the stability. Benzyl chloride appeared to be the least stable, so additions were made every 15 min.; other solutes were allowed periods up to hours. Solids were weighed in; liquids were added from a micrometer syringe calibrated for each liquid.

The lowest reported value for κ_0 is $0{\cdot}85 \times 10^{-6}$ at 99° in an early paper by Klemensiewicz.[1] Klemensiewicz and Balówna [2] combined repeated distillation with fractional freezing *in vacuo* and in general obtained for κ_0 "several units" of 10^{-6}. Jander and Swart,[3] by repeated distillation in dry carbon dioxide, usually obtained $8—12 \times 10^{-6}$ at 99°, their lowest value being $6{\cdot}7 \times 10^{-6}$.

Results and Discussion

(1) *Introductory; Results for* 1-1 *Strong Electrolytes.*—Table 1 shows for each run the equivalent conductance Λ derived from the specific conductance κ at concentrations c of solute; no correction is yet made for the specific conductance κ_0 of the solvent sample. For benzyl chloride, where this correction is large, we quote κ itself.

Conductance results of the highest accuracy would require large quantities of solvent; but liquid antimony trichloride is difficult to purify, corrosive, hygroscopic, and poisonous, so large-scale work would involve major difficulties in design. We aimed therefore at a general small-scale survey of this new field of organic ionisations to an accuracy of about

Table 1. *Conductance results (uncorrected for* κ_0*) at 75°. (c throughout in millimoles/l.;* Λ *in usual units.)*

Triphenylmethyl chloride

Run 1. $\kappa_0 = 6{\cdot}6 \times 10^{-6}$										
c ...	2·21	4·16	5·36	8·83	12·4	14·4	20·0	23·5	29·8	41·3
Λ ...	85·5	84·1	83·4	82·0	81·0	80·2	79·1	78·6	77·7	75·9
Run 2. $\kappa_0 = 5{\cdot}20 \times 10^{-6}$										
c ...	3·12	7·95	12·1	16·5	22·9	30·3	38·5	44·7		
Λ ...	85·5	83·5	82·8	81·8	80·8	79·5	78·4	77·5		
Run 3. $\kappa_0 = 5{\cdot}63 \times 10^{-6}$										
c ...	1·45	3·86	7·20	12·5	17·7	22·8	29·4	36·5		
Λ ...	85·9	82·5	80·8	78·9	77·2	76·3	75·0	73·0		

Tetramethylammonium chloride

$\kappa_0 = 6{\cdot}0 \times 10^{-6}$							
c ...	1·56	7·02	10·1	13·9	19·3	26·7	32·9
Λ ...	94·7	90·8	89·1	88·2	87·1	85·8	84·8

Bornyl chloride

Run 1. $\kappa_0 = 5{\cdot}47 \times 10^{-6}$										
c ...	2·37	4·20	7·76	9·95	12·6	16·2	19·5	24·6	32·8	40·5
Λ ...	41·4	40·4	39·0	38·7	38·4	38·2	38·0	37·7	37·9	38·2
Run 2. $\kappa_0 = 4{\cdot}27 \times 10^{-6}$										
c ...	1·54	3·69	5·83	7·85	10·5	12·9	15·5	18·8	24·9	30·5
Λ ...	43·7	40·4	39·3	38·8	38·0	37·6	37·9	37·3	38·1	38·7

n-Decyl chloride

Run 1. $\kappa_0 = 5{\cdot}54 \times 10^{-6}$				
c ...	1·58	3·13	4·69	6·27
Λ ...	37·4	36·2	35·7	35·0

1-Ethylcyclohexyl chloride

Run 1. $\kappa_0 = 4{\cdot}46 \times 10^{-6}$												
c ...	0·82	1·62	3·55	5·35	7·24	9·23	11·2	13·2	16·2	19·3	22·2	26·3
Λ ...	33·2	31·2	28·4	26·5	26·0	25·3	24·9	24·7	24·5	24·3	24·2	24·3
Run 2. $\kappa_0 = 4{\cdot}06 \times 10^{-6}$												
c ...	0·77	1·59	2·40	3·95	5·66	7·37	9·09	10·8	13·4	16·0	18·6	22·2
Λ ...	35·5	31·1	29·5	28·2	26·5	25·6	25·4	24·8	24·4	23·6	23·7	23·2

[1] Klemensiewicz, *Z. phys. Chem.*, 1924, **113**, 28.

TABLE. 1. (*Continued.*)

Cyclohexyl chloride

Run 1. $\kappa_0 = 5{\cdot}29 \times 10^{-6}$									
c ...	3·65	6·22	8·86	11·5	14·0	16·6	20·6	24·6	30·0
Λ ...	18·7	18·6	18·5	18·4	18·6	18·6	18·8	19·0	18·8
Run 2. $\kappa_0 = 5{\cdot}70 \times 10^{-6}$									
c ...	2·12	4·44	6·72	9·06	11·5	13·8	16·3	19·9	
Λ ...	21·80	19·5	18·8	18·5	18·1	18·0	17·8	17·8	
Run 3. $\kappa_0 = 5{\cdot}52 \times 10^{-6}$									
c ...	2·32	4·70	7·02	9·36	11·8	14·1	16·5	20·1	
Λ ...	19·8	19·1	18·9	18·8	18·8	18·9	19·1	19·2	
Run 4. $\kappa_0 = 5{\cdot}33 \times 10^{-6}$									
c ...	1·09	2·34	4·96	7·57	10·24	12·9	15·5	18·1	22·1
Λ ...	24·8	21·0	19·6	18·8	18·7	18·7	18·7	18·8	19·0

Diphenylmethyl chloride

Run 1. $\kappa_0 = 5{\cdot}66 \times 10^{-6}$									
c ...	1·85	3·77	5·71	9·50	13·4	17·1	20·8	25·7	31·5
Λ ...	19·5	17·6	17·0	16·6	16·1	16·1	16·1	16·2	16·4
Run 2. $\kappa_0 = 4{\cdot}23 \times 10^{-6}$									
c ...	1·00	4·18	7·28	13·0	18·6	24·4	31·3		
Λ ...	22·6	18·4	15·9	15·8	16·5	16·9	17·2		
Run 3. $\kappa_0 = 6{\cdot}66 \times 10^{-6}$									
c ...	1·75	3·57	5·33	8·16	11·9	15·7	19·5		
Λ ...	19·8	17·7	17·1	16·4	16·1	15·7	15·5		

Cinnamyl chloride

Run 1. $\kappa_0 = 4{\cdot}14 \times 10^{-6}$									
c ...	0·77	1·79	3·87	7·01					
Λ ...	16·8	12·4	9·97	8·78					
Run 2. $\kappa_0 = 5{\cdot}35 \times 10^{-6}$									
c ...	1·32	3·22	6·33	9·48	13·54	17·8	22·6	26·3	
Λ ...	12·8	10·2	8·73	8·18	7·93	7·87	7·89	8·18	
Run 3. $\kappa_0 = 5{\cdot}29 \times 10^{-6}$									
c ...	2·06	4·45	7·41	11·4	16·9	22·5	29·2		
Λ ...	12·40	9·88	8·43	7·87	7·72	8·00	8·42		

Benzyl chloride (c and κ, the specific conductance)

Run 1. $\kappa_0 = 6{\cdot}17_3 \times 10^{-6}$										
c	2·61	6·33	10·7	15·4	19·8	24·5	29·1	35·3	44·7	
κ ($\times 10^{-6}$) ...	6·96	8·45	10·1	12·3	14·6	17·4	20·6	26·0	47·6	
Run 2. $\kappa_0 = 5{\cdot}19_5 \times 10^{-6}$										
c	4·16	10·6	17·2	24·1	31·2	39·7				
κ ($\times 10^{-6}$) ...	6·50	9·02	12·0	16·7	27·6	41·4				
Run 3. $\kappa_0 = 4{\cdot}67_8 \times 10^{-6}$										
c	6·81	12·4	18·4	24·3	30·1	36·0	41·8			
κ ($\times 10^{-6}$) ...	8·24	10·5	13·20	16·5	21·4	30·6	42·9			

1%; this was almost, but not quite achieved. Even so the interpretation of the results demands the consistent application of ionic-atmosphere (Debye–Hückel) theory, for our results extend up to ionic strengths (~0·03N) where interionic-force corrections to conductance and to activity amount to tens rather than units %.

Two of the solutes chosen, triphenylmethyl chloride and tetramethylammonium chloride, are typical 1-1 strong electrolytes at 75°. In Fig. 1 we plot Λ against $\sqrt{c}$ for these; Λ approaches Λ_0 with the theoretical Debye–Hückel–Onsager slope X given by

$$X = (0{\cdot}661\Lambda_0 + 29{\cdot}74) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where

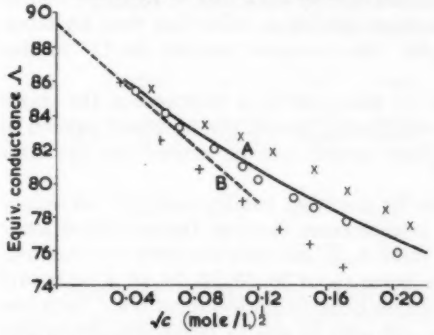
$$\Lambda = \Lambda_0 - X\sqrt{c} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(In calculating X the viscosity coefficient [6] η is taken as 0·0258 c.g.s. unit and the dielectric constant [7] as 33·2.) For more concentrated solutions the results agree with the theoretical first approximation of Falkenhagen, Leist, and Kelbg,[8] *viz.*,

$$\Lambda = \Lambda_0 - X\sqrt{c}/(1 + Y\sqrt{c}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

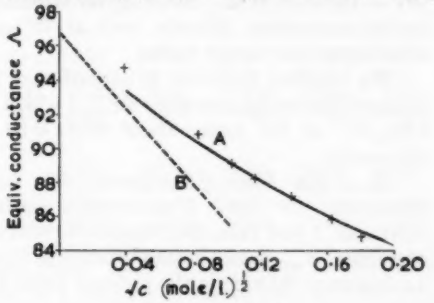
the curves drawn in Figs. 1 and 2, the values for Λ_0 (89·4, 96·9) and Y (1·95, 2·4) for triphenylmethyl and tetramethylammonium chloride, respectively, being obtained by successive approximation using the theoretical value for X. While this work was in progress Jander and Swart [3] showed, for more concentrated solutions at 99°, that Λ for triphenylmethyl chloride was only a few units % lower than for potassium, ammonium, or tetramethylammonium chloride; as shown in Part I, the freezing-point data for tetramethylammonium, triphenylmethyl, cæsium, and potassium chloride, and the conductance

FIG. 1. *Plot of equivalent conductance against (concentration)$^{\frac{1}{2}}$ for triphenylmethyl chloride.*



A, line represents eqn. (3). B, *line represents Debye–Hückel–Onsager equation.* ○, ×, + *runs* 1, 2, 3.

FIG. 2. *Plot of equivalent conductance against (concentration)$^{\frac{1}{2}}$ for tetramethylammonium chloride.*



A, B *as in* Fig. 1.

data of Klemensiewicz and Balówna [2] for potassium, ammonium, rubidium, and thallium chloride at 99° all agree well with the expectations for 1-1 strong electrolytes.

This mass of data shows, therefore, (*a*) that there are 1-1 strong electrolytes in this solvent, and (*b*) that triphenylmethyl chloride is one of them; and it proves the mode of ionisation of the chlorine. In principle RCl could ionise:

$$RCl + SbCl_3 \rightleftharpoons R^+ + SbCl_4^-$$
$$2RCl + SbCl_3 \rightleftharpoons 2R^+ + SbCl_5^{2-}$$
$$3RCl + SbCl_3 \rightleftharpoons 3R^+ + SbCl_6^{3-}, \text{ etc.}$$

and solid addition compounds between alkali chlorides and antimony trichloride are known corresponding to these complex modes. But they are incompatible with either the freezing-point or the conductance data in solution; even the second scheme would imply a limiting van't Hoff factor i of 1·5, and a limiting Onsager slope about three times greater than for a 1-1 electrolyte.

Finally, the results for tetramethylammonium chloride confirm the abnormal mobility of the Cl^- ($SbCl_4^-$) ion in $SbCl_3$; Cl^- is also abnormally mobile in arsenic trichloride.[9] This point is so important to the further discussion that we repeat here the evidence:

(*a*) the transport number of Cl^- in potassium and ammonium chloride solutions at 99°

[7] Schlundt, *J. Phys. Chem.*, 1901, **5**, 503.
[8] Falkenhagen, Leist, and Kelbg, *Ann. Physik*, 1952, **11**, 51.
[9] Gutmann, *Svensk Kem. Tidskr.*, 1956, **68**, 1.

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was directly measured at about 0·9 by Frycz and Tolloczko,[10] using Hittorf's method, and in general a high value is suggested by the small variation in Λ from chloride to chloride.[2]

(*b*) Jander and Swart [3] have shown that a conductivity titration curve like that of a strong acid–strong base reaction in water is obtained if triphenylmethyl or potassium chloride in antimony trichloride is titrated with antimony pentachloride at 80°. The explanation is that the reaction is:

$$SbCl_4^- + SbCl_5 \longrightarrow SbCl_3 + SbCl_6^-$$

with $SbCl_4^-$ abnormally mobile and $SbCl_6^-$ not. If $SbCl_6^-$ and the cations are about equally mobile, these data imply a transport number 0·86 for Cl^- in triphenylmethyl chloride.

(*c*) Thirdly, our own result for tetramethylammonium chloride confirms these conclusions. For a large number of non-hydroxylic solvents and at many temperatures the Walden product $\lambda_0\eta$ of NMe_4^+ is about 0·3$_4$ (Landolt–Börnstein's tables), the highest recorded value being about 0·45; for these two cases the mobility of NMe_4^+ in antimony trichloride at 75° must be 13 or 18 and the transport number of Cl^- (97 − 13)/97 = 0·87 or (97 − 18)/97 = 0·82. Since Λ_0 for triphenylmethyl chloride is rather less than for tetramethylammonium chloride, both at 75° and 99°, the transport number for Cl^- in this electrolyte must be yet higher.

We consider therefore as proved that the Cl^- exists in these solutions as the singly charged species (presumably $SbCl_4^-$) which is abnormally mobile, the transport number in $CPh_3^+Cl^-$ at 75° being about 0·85—0·90. These points will be needed for the later discussion.

(2) *A New Mode of Ionisation.*—The results for the other halides cannot be so simply explained; for Table 1 shows as a general phenomenon that, as the concentration c increases, Λ first falls, then reaches a constant value $\Lambda_{min.}$, and then increases very slightly. Moreover, $\Lambda_{min.}$ varies greatly from case to case, being about 38, 35, 24, 18, 16, 8 for bornyl to cinnamyl chloride in the order of Table 1, and for benzyl chloride about 0·6. Such low values of Λ, varying so much from case to case, can only be due to incomplete ionisation. But incomplete ionisation in the obvious simple mode $RCl \rightleftharpoons R^+ + Cl^-$ would imply that Λ should fall greatly as c increases; this consequence is completely contradicted by the facts. To take but one example: for diphenylmethyl chloride $\Lambda \simeq 19$ at 2×10^{-3}N; Ostwald's dilution law would predict $\Lambda \simeq 5$ at 30×10^{-3}N, where in fact $\Lambda \simeq 16$.

Table 1 shows this to be a general phenomenon and it can easily be shown that no reasonable assumption about interionic-force effects could remove so gross a discrepancy.

We must therefore explain how an apparent degree of ionisation, much less than unity and varying from case to case, can yet be almost independent of concentration. The law of mass action, neglecting interionic-force effects, can explain this if, and only if, x covalent solute molecules give an equal number x of ions with the paradoxical consequence that such an electrolyte might be almost completely ionised yet give a normal freezing-point depression; this consequence is supported by some freezing-point data by Dr. G. B. Porter.[11]

There are, of course, various ways in which this could happen. The simplest are the pair–pair ionisations

$$2RCl \rightleftharpoons R_2Cl^+ + Cl^- \text{ (cation-association)}$$
$$2RCl \rightleftharpoons R^+ + RCl_2^- \text{ (anion-association)}$$

If, of course, both these processes occur at once

$$3RCl \rightleftharpoons R_2Cl^+ + RCl_2^- \text{ (bilateral association)}$$

then Λ should increase with increasing c. The small observed increase at higher values of c will be quantitatively explained as an interionic-force effect, so that one or other of the

[10] Frycz and Tolloczko, *Festschrift Univ. Lwów*, 1912, **1**, 1; *Chem. Zentr.*, 1913, I, 91.
[11] Porter, unpublished work in these laboratories.

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pair–pair ionisations should be involved. A choice in favour of the first can be made for two reasons: (*a*) *General chemical reasons* (see below). (*b*) *Mobility.* We have shown that Cl^- ($SbCl_4^-$) is abnormally mobile in antimony trichloride. In general, if a foreign molecule has a greater affinity for an abnormally mobile solvent-ion than has the solvent itself, the new complex ion is not abnormally mobile; thus $SbCl_6^-$ and $AlCl_4^-$ are not abnormally mobile [3] in antimony trichloride; nor is OH_3^+ abnormally mobile in methanol or ethanol,[12] nor is NH_4^+ in water. If, therefore, RCl has a greater affinity for Cl^- than has antimony trichloride, the ion RCl_2^- should not be abnormally mobile; if it has not, the ion should not exist significantly, since the trichloride is in enormous excess.

(3) *Strong Electrolytes in this New Mode*: *Bornyl Chloride, Decyl Chloride.*—Now for some of these electrolytes Λ is about half that of the 1-1 electrolytes containing the abnormally mobile Cl^- ion. The explanation is that there are about half as many Cl^- ions (cation-association); alternatively, we would have to suppose a new anion also abnormally mobile but not so much. This is improbable.

TABLE 2. *Comparison of* Λ_B *for bornyl chloride at concentrations* c_B (mmoles/l.) *with* Λ^* *for triphenylmethyl chloride.*

Run 1.									
C_B	2·37	4·20	7·76	9·95	12·63	16·21	19·54	24·59	31·81	40·53
Λ_B	41·4	40·4	39·1	38·7	38·4	38·2	38·0	37·7	37·9	38·2
Λ_B/Λ_0^*...	0·463	0·452	0·457	0·434	0·430	0·427	0·425	0·422	0·424	0·427
Λ_B/Λ_C^*	0·479	0·472	0·462	0·461	0·461	0·461	0·462	0·463	0·464	0·472
Run 2.										
C_B	1·54	3·69	5·83	7·85	10·52	12·85	15·53	18·82	24·95	30·47
Λ_B	43·7	40·4	39·3	38·8	38·0	37·6	37·9	37·3	38·1	38·7
Λ_B/Λ_0^*...	0·489	0·452	0·440	0·434	0·425	0·421	0·424	0·417	0·426	0·433
Λ_B/Λ_C^*	0·502	0·482	0·462	0·459	0·454	0·451	0·457	0·454	0·469	0·480

Considering therefore the cation-association mode, a strong electrolyte in this mode would give exactly half as many chlorine ions as a strong electrolyte such as triphenylmethyl chloride which ionises in the simple mode. As the mobility of the cation is of minor importance, a strong electrolyte in the cation-association mode should give a $\Lambda \approx \frac{1}{2}\Lambda^*$ over the whole concentration range, where Λ^* is the value of Λ for a strong electrolyte in the simple mode (of which we take triphenylmethyl chloride as an example). This simple consequence may easily be compared with fact. Let us consider bornyl chloride, for which Λ is the highest. In Table 2 we show the values of Λ_B, its equivalent conductance at concentration c_B, divided by Λ_0^* for triphenylmethyl chloride (89·4; equation 3). This ratio is rather less than $\frac{1}{2}$ and drifts by only about 10% over a thirty-fold variation in c_B. If, however, this interpretation be correct, the agreement with experiment should be improved if account is taken of interionic-force effects; this can be done approximately by replacing Λ_0^* by Λ_C^*, the value of Λ^* for triphenylmethyl chloride at a concentration one-half of C_B (equation 3). The values of this new ratio are given in the last line of Table 2.

The drift is now almost completely removed except for the most dilute points (where the solvent correction is appreciable), and the mean value

$$\Lambda_B/\Lambda_C^* = 0{\cdot}467 \pm 0{\cdot}006 \text{ (median error)} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

is in excellent agreement with the predictions for complete cation-association ionisation: (*a*) Λ_B/Λ_C^* independent of concentration, (*b*) $\Lambda_B/\Lambda_C^* \approx \frac{1}{2}$. This ratio should not be exactly $\frac{1}{2}$ unless the two cation mobilities were exactly equal; it should not be much different as they are small compared with the anion mobilities; it should even be rather less than $\frac{1}{2}$ as (dibornyl chloride)$^+$ is bigger and presumably slower than (triphenylmethyl)$^+$.

Similarly for the four (Λ_D) points for n-decyl chloride, Λ_D/Λ_C^* is 0·431, 0·420, 0·417,

[12] Goldschmidt and Dahll, *Z. phys. Chem.*, 1924, **108**, 121; 1924, **114**, 1; Murray-Rust and Hartley, *Proc. Roy. Soc.*, 1929, *A*, **126**, 84.

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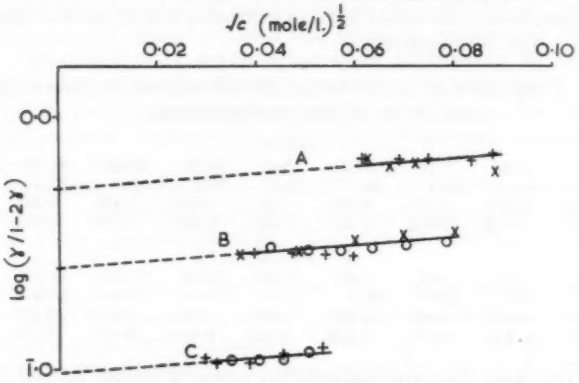
0·413; this solute also must be almost, but perhaps not quite, completely ionised in the cation-association mode. We would emphasise the statistical fact that there exist two clusters of Λ values: (*a*) at 70—90 for triphenylmethyl, tetramethylammonium, and the alkali chlorides;[6] (*b*) at 15—40 for bornyl, decyl, the two cyclohexyl, and diphenylmethyl chlorides, with (*c*) none in between. This is naturally explained if the limiting Λs in these two clusters represent strong electrolytes in different modes.

(4) *Incomplete Ionisation in This Mode (Other Chlorides except Benzyl).*—The other solutes show, above a certain concentration, Λ roughly constant which would be expected from incomplete ionisation in the mode $2RCl \rightleftharpoons R_2Cl^+ + Cl^-$. The first approximation is to suppose that this is the only ionisation involved, whence $(R_2Cl^+) = (Cl^-)$, and to

FIG. 3. *Plot of* $\log(\gamma/1-2\gamma)$ *against* $(concentration)^{\frac{1}{2}}$.



A, 1-*Ethylcyclohexyl*; B, *diphenylmethyl*; C, *cinnamyl*.

obtain (Cl^-) from the observed Λ and that, Λ*, of the standard electrolyte triphenylmethyl chloride. Let c be the concentration of the chloride considered, and let γc be that of the chlorine anion; then

$$(R_2Cl^+)(Cl^-)/(RCl)^2 = K_0 = \gamma^2/(1-2\gamma)^2 \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Identifying the supposedly constant value of γ with $\Lambda_{min.}/\Lambda_0^*$ where $\Lambda_{min.}$ is the value at the shallow minimum in the Λ–c curve, we obtain the following first approximations for K_0: 1-ethylcyclohexyl chloride $0{\cdot}3_4$, cyclohexyl chloride $0{\cdot}1_2$, diphenylmethyl chloride $0{\cdot}07_8$, cinnamyl chloride $0{\cdot}01_1$.

In this treatment, where the effects of interionic forces are neglected, it is predicted that Λ should be exactly constant; in fact it is only roughly so. For weak electrolytes, Debye–Hückel theory should come in, first, in the effect of ionic strength on mobility, tending to reduce Λ with increasing c (as with bornyl chloride) and, secondly, in the effect on activity coefficients, tending to increase Λ; the second is the larger effect. These corrections are made as follows:

Let the observed value Λ_c of Λ at a given total solute concentration c correspond to an ionic concentration c_i. Let Λ_i^* be the Λ* for the standard electrolyte triphenylmethyl chloride at the same ionic concentration c_i^*. Since this chloride is a strong electrolyte, for this, $c_i^* = c^*$. We take $\gamma = \Lambda_c/\Lambda_i^*$; Λ_i^* can easily be obtained graphically by successive approximation. Considering the ionic activity coefficients f we have

$$\gamma^2 f^2/(1-2\gamma)^2 = K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

from the Debye-Hückel limiting law

$$\log_{10} f = -1{\cdot}46\sqrt{c_i} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Hence

$$\log_{10}[\gamma/(1-2\gamma)] = \tfrac{1}{2}\log_{10} K + 1{\cdot}46\sqrt{c_i} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

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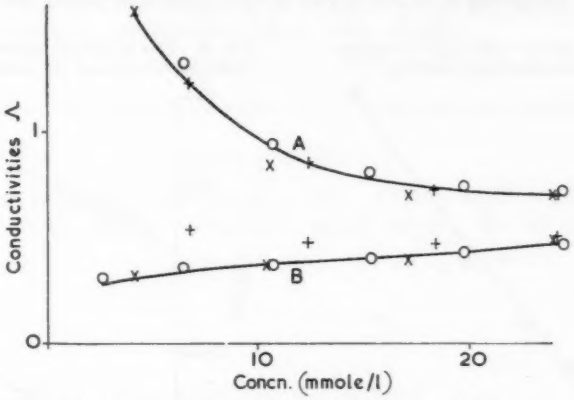
In Fig. 3 we plot for the more concentrated points $\log_{10}[\gamma/(1-2\gamma)]$ against $\sqrt{c_i}$, the lines drawn having the theoretical slope. As the points lie fairly well about the theoretical lines, the small rises in Λ in the concentrated solutions have been explained. The values of K so obtained are: 1-ethylcyclohexyl chloride 0·27, cyclohexyl chloride 0·10, diphenylmethyl chloride 0·063, cinnamyl chloride 0·0093 (10—20% corrections on K_0).

The single assumption therefore of a new mode of ionisation $2RCl \rightleftharpoons R_2Cl^+ + Cl^-$ predicts roughly constant values of Λ with an upper limit $\sim\frac{1}{2}\Lambda^*$ to which bornyl and decyl chloride are a good approximation. The same hypothesis, when refined by the Debye–Hückel corrections, explains quantitatively the small decrease of Λ with concentration for bornyl chloride, and the small rise in Λ in the stronger solutions of the weaker electrolytes. Evidently, however, it cannot explain the initial fall in Λ to its minimum value $\Lambda_{min.}$; in dilute solutions of the weaker electrolytes Λ is too high by about 50%.

FIG. 4. *Plot of concentration against conductivities for benzyl chloride.*



A, $\Lambda_{uncorr.}$. B, $\Lambda_{sub.}$. At $c = 2{\cdot}6$, $\Lambda_{uncorr.} = 2{\cdot}68$.

(5) *Effects of Solvent Conductance and of Simple Ionisation (Benzyl Chloride).*—In dilute solutions the self-conductance of the solvent must certainly be of importance, and possibly also the simple mode $RCl \rightleftharpoons R^+ + Cl^-$, which is the principal mode for triphenylmethyl chloride. The results for benzyl chloride provide a convenient case; the degree of ionisation is small (~1%); hence ionic-strength effects can be neglected and concentration (RCl) of un-ionised chloride equated to c the stoicheiometric concentration, and the self-conductance κ_0 is a major effect (for the four most dilute points $\kappa_0/\kappa = 89$, 80, 75, and 57%, respectively).

The mathematically simplest ways to allow for the solvent conductance are to make no correction at all or to subtract κ_0 from κ in full, thus obtaining two extremes $\Lambda_{uncorr.}$ and $\Lambda_{sub.}$. These are plotted against c in Fig. 4; $\Lambda_{uncorr.}$ falls from about 2·5 to 0·7 while $\Lambda_{sub.}$ rises from 0·3 to 0·5, the two estimates approaching a roughly constant value of about 0·55, corresponding to $3{\cdot}8 \times 10^{-5}$ for the equilibrium constant K_0.

It appears that the full correction is too large for the dilute solutions. To improve it demands an understanding of the cause [13] of κ_0. Simple subtraction implies that the ionisations of the solvent and solute produce no common ion; this seems unlikely here. The facts detailed in the Experimental section suggest strongly that the conductance of antimony trichloride is in fact principally due to impurities (cf. Klemensiewicz and Balówna [2]), some volatile ($AsCl_3$?, an ammonium salt?), and some increasing rapidly at 99° but slowly at 75° and so probably impurity from the glass. These would both probably

[13] Wynne-Jones, *J. Phys. Chem.*, 1927, **31**, 1647.

produce the Cl^- ($SbCl_4^-$) anion, so the most likely hypothesis is that the self-conductance is principally—we assume entirely—due to strong-electrolyte impurities with the Cl^- anion.

This view implies that the self-conductance κ_0 immediately gives the concentration of impurity cation P^+, roughly constant throughout a run. The conductance κ of the solution at concentration c gives directly the total (Cl^-), as the cation is of minor importance. It can be shown (see Appendix) that in this limiting case

$$[(Cl^-) - (P^+)]\,(Cl^-)/c = K' + Kc \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where K' and K are the equilibrium constants

$$(R^+)(Cl^-)f^2/(RCl) = K' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$(R_2Cl^+)(Cl^-)f^2/(RCl)^2 = K \text{ (as before)} \quad . \quad . \quad . \quad \text{(equiv. to 6)}$$

Fig. 5 shows $[(Cl^-) - (P^+)](Cl^-)/c$ plotted against c for benzyl chloride; the points fall round a straight line giving $K = 3{\cdot}7 \times 10^{-5}$, $K' \approx 1 \times 10^{-7}$ (the latter uncertain to about

FIG. 5. *Plot of* $[(Cl^-) - (P^+)](Cl^-)/c$ *against concentration for benzyl chloride.*

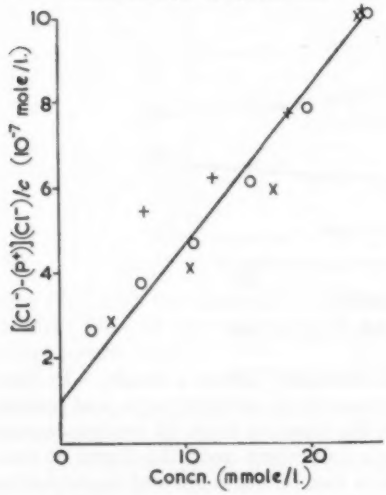
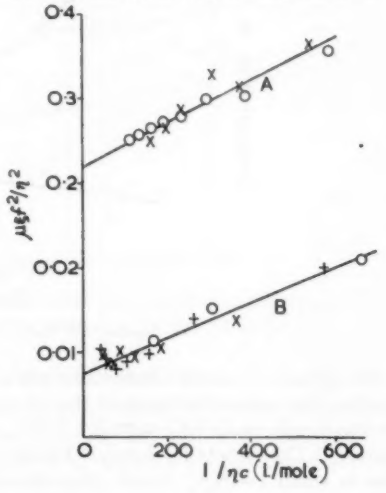


FIG. 6. *Plot of* $\mu\xi f^2/\eta^2$ *against* $1/\eta c$ *for* (A) *1-ethylcyclohexyl and* (B) *cinnamyl chloride.*



$\pm 50\%$). The value of K thus obtained for the whole range agrees with the previous limiting value (Fig. 4), and the non-zero intercept suggests that the simple mode of ionisation is just about detectable. Essentially the same value of K' is obtained if one assumes the whole of κ_0 to be due to the equilibrium $2SbCl_3 \rightleftharpoons SbCl_2^+ + SbCl_4^-$, but a considerably smaller value if one simply subtracts the solvent correction (*i.e.*, supposes that the anion responsible for κ_0 is not $SbCl_4^-$).

(6) *General Equation.*—Having thus analysed the conductance–composition curve in terms of a complex (R_2Cl^+, Cl^-) and a simple mode (R^+, Cl^-) of ionisation and the effect of strong-electrolyte impurity, it is possible to work out the consequences of these ideas in the general case where interionic-force effects matter and where the degree of ionisation is not small. This requires no new arguments and is given in an Appendix (cf. Wooster [14]). In Fig. 6 we show for the two extreme cases of 1-ethylcyclohexyl and cinnamyl chloride the graph of $\mu\xi f^2/\eta^2$ against $1/\eta c$; good straight lines are obtained.

(7) This analysis gives therefore the values of the two dissociation constants K' and K

[14] Wooster, *J. Amer. Chem. Soc.*, 1938, **60**, 1609.

which are shown in Table 3. The errors quoted are random errors; systematic errors of 10% or so may arise through approximations in the treatment, but should affect all solutes alike.

TABLE 3.

Chloride	K	K'
Triphenylmethyl	—	S.E. (>0·2) *
Bornyl (n-decyl)	S.E.	—
1-Ethylcyclohexyl	$2·2 \pm 0·1 \times 10^{-1}$	$2·5 \pm 0·6 \times 10^{-4}$
Cyclohexyl	$9·7 \pm 0·2 \times 10^{-3}$	$4·1 \pm 1·2 \times 10^{-4}$
Triphenylmethyl	$5·8 \pm 0·3 \times 10^{-2}$	$2·6 \pm 1·5 \times 10^{-5}$
Cinnamyl	$7·5 \pm 0·5 \times 10^{-3}$	$2·1 \pm 0·8 \times 10^{-5}$
Benzyl	$3·7 \pm 0·4 \times 10^{-5}$	$1·0 \pm 0·5 \times 10^{-7}$

S.E. = Strong electrolyte.
* The estimate for K' for CPh_3Cl is based on the assumption that 10% of undissociated CPh_3Cl would be just detectable.

(8) In Fig. 7 the rather uncertain values of log K' are plotted against log K. As can be seen, they lie around a straight line of slope unity, whence

$$\log_{10}(K/K') = +2·95 \pm 0·40 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

The ratio of these two equilibrium constants is, evidently, the equilibrium constant χ given by

$$\chi = (R_2Cl^+)/(RCl)(Cl^-) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

This process has, therefore, a standard free energy $\Delta G° = -4·57T \times 2·95 = -4·7 \pm 0·6$ kcal./mole, which is, roughly, independent of the solute. We can thus immediately

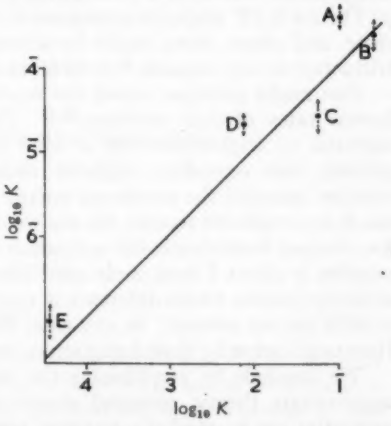


FIG. 7. *Plot of* $\log_{10} K'$ *against* $\log_{10} K$.
A, *Cyclohexyl*; B, *ethylcyclohexyl*; C, *diphenylmethyl*; D, *cinnamyl*; E, *benzyl*.

explain why the complex mode is undetectable for triphenylmethyl chloride; for (Appendix, eqn. A10) the ratio of (R^+) to (R_2Cl^+) is inversely as the proportion of unionised RCl which for this solute is very small. It is probable that this effect is enhanced by peculiar repulsion effects.[15]

(9) *Conclusion.*—The results obtained agree to within the limits of their experimental error with the hypothesis of complex and simple ionisation; simple ionisation alone could not represent them to within a factor of 2; and they cannot be explained as due to the obvious side reactions—olefin formation, condensation—since these give hydrogen chloride which in this solvent is effectively a non-conductor.[16]

It is therefore almost certain that carbonium-ion formation has been observed; and such equilibrium ionisations, though not for simple aliphatic systems, have already been

[15] Baughan, *Discuss. Faraday Soc.*, 1947, **2**, 70.
[16] Klemensiewicz and Zebrówska, *Roczniki Chem.*, 1934, **14**, 14.

Vol. 1961, page 1721, Table 3, 5th item. *For* Triphenylmethyl *read* diphenylmethyl; equation (12) *should read* $\chi = (R_2Cl^+)/(RCl)(Cl^-)$.

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measured in hydrofluoric [17] and in sulphuric acid.[18] These facts, however, were predictable. For Baughan, Evans, and Polanyi [19] showed that the activation energy of carbonium ionisations (S_N1 reactions in Ingold's terminology [20]) should be for simple cases about equal to the endothermicity of the reaction, and enough is now known about such activation energies, particularly from the work of Ingold, Hughes, and their co-workers,[20] to make it clear that an extra solvation energy of only a few kcal. should make equilibrium ionisation detectable. In theory, antimony trichloride should be a peculiarly favourable solvent, since the dielectric constant is high and the affinity $Cl^- + SbCl_3 \longrightarrow SbCl_4^-$ considerable; in fact, it is peculiarly favourable since triphenylmethyl chloride is a strong electrolyte while even in sulphur dioxide its dissociation constant [21] to R^+ and Cl^- is $10^{-4\cdot4}$ (at 0°). And these same energetic calculations [19] predict the absence of olefin-formation; for the proton affinity of an olefin is very large (152 kcal./mole for ethylene [22]) so that reactions such as $C_2H_5 + Y \longrightarrow YH^+ + CH_2{:}CH_2$ will not happen unless Y also has a high proton affinity (that of water is 182 kcal./mole; [23] that of alcohols about the same) and there is no reason to suppose this for antimony trichloride.

The discovery of equilibrium carbonium ionisations in this solvent was in effect the verification of order-of-magnitude predictions already made. The strange feature is that the ionisation by the simple mode is so enhanced by the reaction

$$R^+ + RCl \longrightarrow R_2Cl^+ (\Delta G^\circ \simeq -5 \text{ kcal./mole});$$

of this various explanations are possible: (*a*) As the charge-bearing radius of the simple carbonium ion is effectively very small since the ion is planar, the association may be a simple ion-dipole effect. (*b*) The carbonium ion is an electron-deficient structure like BH_3 and evidence has been accumulating [24,25] to suggest addition reactions from this cause. (*c*) The ion R_2Cl^+ might be analogous to the diaryliodonium ions. The distinction between these, and other, views might be solved by infrared measurements for which antimony trichloride is very suitable,[26] or in other ways.

One might perhaps expect the equilibrium constants obtained to correlate with the known rates of S_N1 reactions.[20,27] The order benzyl < diphenylmethyl < tertiary aliphatic ⩽ triphenylmethyl is what might be expected; the high ionisations of the primary and secondary aliphatic chlorides are, however, surprising. But activation energies measure the maximum energy in the reaction path, and any rearrangement of bonds in, or solvent around, the ion would make this differ from the endothermicity; even for covalent bond-fission the activation energy of the dissociation of hexaphenylethane in solution is about 7 kcal./mole more than the endothermicity. The short-chain primary aliphatic halides, whose difference in reactivity has been so instructive,[20] are inconveniently volatile for our solvent; in any case, their differences will probably be " levelled " off in Hantzsch's sense by their being strong electrolytes.

We conclude by emphasising the main result of this work. We have, following an approximate theory, obtained simple carbonium ions in bulk where their equilibrium properties can be studied; previous knowledge of these interesting species has depended on indirect inferences from reaction kinetics.

We are indebted to a Government Research Fellowship which allowed one of us (A. G. D.) to take part in this work.

[17] Kilpatrick and Luborsky, *J. Amer. Chem. Soc.*, 1953, **75**, 577.
[18] Newman and Deno, *J. Amer. Chem. Soc.*, 1951, **73**, 3644.
[19] Baughan, Evans, and Polanyi, *Trans. Faraday Soc.*, 1941, **37**, 377.
[20] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953.
[21] Pocker, *Proc. Chem. Soc.*, 1959, 386.
[22] Calculations as by Baughan, Evans, and Polanyi (ref. 19), but with the ionization potential of C_2H_5 taken as 200 kcal./mole (Stevenson, *Trans. Faraday Soc.*, 1953, **49**, 867).
[23] Sherman, *Chem. Rev.*, 1932, **11**, 93.
[24] Dewar, *Ann. Reports*, 1951, **48**, 122.
[25] Pauling, " The Nature of the Chemical Bond," Oxford Univ. Press, 1960, p. 383.
[26] Lacher, Croy, Kianpour, and Park, *J. Chem. Phys.*, 1954, **58**, 206.
[27] Streitwieser, *Chem. Rev.*, 1956, **56**, 571.

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Appendix: Solution of the general problem.

(*a*) The first stage is to obtain for each point the chloride-ion concentration (Cl^-) from graphical solution of equation (3) and from this the activity coefficient f from equation (7). Equally the chloride-ion concentration in the pure solvent is obtained and put equal to (P^+), the concentration of impurity cation.

(*b*) The following relations hold between the concentrations:

$$(Cl^-) = (P^+) + (R_2Cl^+) + (R^+) \text{ (electrical neutrality)} \quad . \quad . \quad . \quad . \quad \text{(A1)}$$

$$c = (RCl) + (R^+) + 2(R_2Cl^+) \text{ (stoicheiometry of RCl)} \quad . \quad . \quad \text{(A2)}$$

where c is the total concentration of RCl solute; and we have the two equations of thermodynamic equilibrium:

$$(R_2Cl^+)(Cl^-)f^2/(RCl)^2 = K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(A3)}$$

$$(R^+)(Cl^-)f^2/(RCl) = K' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(A4)}$$

(*c*) It is throughout assumed that A gives (Cl^-) directly, since the cation mobilities are small; it is therefore convenient to express our quantities in terms of (Cl^-), thus:

$$(Cl^-) - (P^+) = (R_2Cl^+) + (R^+) = K(RCl)^2/(Cl^-)f^2 + K'(RCl)/(Cl^-)f^2$$

or

$$[(Cl^-) - (P^+)](Cl^-)f^2 = K(RCl)^2 + K'(RCl) \quad . \quad . \quad . \quad . \quad . \quad \text{(A5)}$$

the fundamental equation.

(*d*) For benzyl chloride, which is very slightly ionised, $(RCl) \approx c, f \approx 1$, whence (A5) becomes

$$[(Cl^-) - (P^+)]\,(Cl^-)/c = K' + Kc \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(A6)}$$

This is equation (9) in this paper (Fig. 5).

(*e*) The more general case can be successively approximated as follows:
Define dimensionless ratios:

$$\left.\begin{array}{l} (Cl^-)/c \equiv \xi;\ [(Cl^-) - (P^+)]/c \equiv \mu;\ \text{these are easily evaluated} \\ (R^+)/c \equiv \alpha;\ (R_2Cl^+)/c \equiv \gamma;\ (RCl)/c \equiv \eta \\ (R^+)/(R_2Cl^+) = \alpha/\gamma \equiv \psi \end{array}\right\} \quad . \quad . \quad \text{(A7)}$$

(A5) now becomes

$$\mu\xi f^2/\eta^2 = K'/\eta c + K \text{ (cf. Fig. 6)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(A8)}$$

and

$$\eta = 1 - \mu(\psi + 2)/(\psi + 1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(A9)}$$

Evidently at $\psi = 0$ (no R^+), $\eta = 1 - 2\mu$, and at $\psi = \infty$ (no R_2Cl^+) $\eta = 1 - \mu$. As most of the organic cation in the stronger solutions appears to be (R_2Cl^+), and as μ in the extreme is only about 0·3, η is not very sensitive to ψ. We obtain therefore first approximations K' and K_1 by (A8) with $\eta = (1 - 2\mu)$. This can then be refined as follows:

From (A3) and (A4)

$$\eta = K'/Kc\psi \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(A10)}$$

whence from (A9)

$$K'/Kc = \psi\,[1 - \mu(\psi + 2)/(\psi + 1)] \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(A11)}$$

This quadratic in ψ can be solved for each point by using the first approximation for K_1'/K_1, thus obtaining η for each point. (A8) can then be replotted by using these new values of η and K_2', K_2 obtained, and the whole, if necessary, repeated. Three approximations were needed for 1-ethylcyclohexyl chloride, two for the other solutes (see Fig. 6).

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335. *Conjugated Cyclic Hydrocarbons and Their Heterocyclic Analogues. Part V.*[1] *1-1′-Azulenylmethyleneazulenium Salts and 1-Ethoxymethyleneazulenium Salts.*

By E. C. Kirby and D. H. Reid.

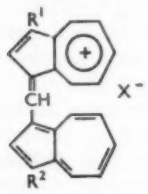
1-1′-Azulenylmethyleneazulenium salts have been synthesised by the condensation of azulenes with (A) 1-formylazulenes in the presence of strong acids and (B) 1-ethoxymethyleneazulenium salts.

Depending upon their degree of substitution, azulenes condense with ethyl orthoformate in the presence of strong acids to give either symmetrical 1-1′-azulenylmethyleneazulenium salts or substituted 1-ethoxymethyleneazulenium salts.

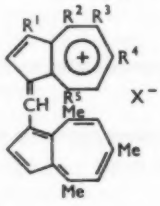
1-Ethoxymethyleneazulenium salts are hydrolysed quantitatively by water to 1-formylazulenes.

Light absorption data for the dye salts are reported.

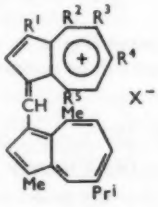
In Part II [2] of this series it was shown that azulenes condense with aromatic aldehydes in the presence of perchloric acid to form 1-(substituted methylene)azulenium perchlorates. With 1-formylazulene, azulene and guaiazulene (7-isopropyl-1,4-dimethylazulene) gave, respectively, 1-1′-azulenylmethyleneazulenium perchlorate (II) and 1-1′-azulenylmethylene-5-isopropyl-3,8-dimethylazulenium perchlorate (XII), members of a new class of dye salts. These compounds represent the only known class of polymethine dye salts whose cations contain carbon alone. We now report further synthetic studies of this class of compounds.



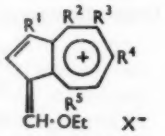
	R^1	R^2	X
(I)	H	H	Cl
(II)	H	H	ClO_4
(III)	Me	H	ClO_4
(IV)	Me	Me	Br
(V)	Me	Me	ClO_4



	R^1	R^2	R^3	R^4	R^5	X
(VI)	H	H	H	H	H	ClO_4
(VII)	Me	H	H	H	H	ClO_4
(VIII)	H	Me	H	Me	Me	ClO_4
(IX)	Me	H	Pr^i	H	Me	ClO_4



	R^1	R^2	R^3	R^4	R^5	X
(X)	H	H	H	H	H	Br
(XI)	H	H	H	H	H	I
(XII)	H	H	H	H	H	ClO_4
(XIII)	Me	H	H	H	H	Br
(XIV)	Me	H	Pr^i	H	Me	ClO_4



	R^1	R^2	R^3	R^4	R^5	X
(XV)	H	H	H	H	H	ClO_4
(XVI)	H	Me	H	Me	Me	Br
(XVII)	H	Me	H	Me	Me	I
(XVIII)	H	Me	H	Me	Me	ClO_4
(XIX)	Me	H	Pr^i	H	Me	Br
(XX)	Me	H	Pr^i	H	Me	
(XXI)	Me	H	Pr^i	H	Me	ClO_4

The method [2] of condensing an azulene with a 1-formylazulene in the presence of perchloric acid was found to be widely but not generally applicable. All condensations with 1-formylazulene and 1-formyl-3-methylazulene were successful. However, 1-formyl-4,6,8-trimethylazulene either reacted incompletely or gave products difficult to purify, while 3-formylguaiazulene (1-formyl-5-isopropyl-3,8-dimethylazulene) failed to condense (see also Kirby and Reid [2]). The desired products were obtained in certain cases by exchanging the rôles of the azulene nuclei of the reactants. Thus, while 3-formylguaiazulene failed to condense with azulene, 1-formylazulene condensed smoothly with guaiazulene to give the salt (XII).[2] This circumvention failed in the attempted preparation of salts [*e.g.*, (IX)], both of whose azulene components give rise to unreactive aldehydes.

The low reactivity of 3-formylguaiazulene and 1-formyl-4,6,8-trimethylazulene in these

[1] Part IV, Kirby and Reid, *J.*, 1961, 163.
[2] Kirby and Reid, *J.*, 1960, 494.

condensations is undoubtedly due to deactivation of the protonated aldehyde function by the electron-releasing alkyl substituents (see also Kirby and Reid [1]).

In agreement with the formulation of these dye salts as resonance hybrids, the condensation product from azulene with 1-formyl-3-methylazulene was identical with that from 1-methylazulene with 1-formylazulene, namely, (III).

1-Formylazulene and 1-formyl-3-methylazulene condensed readily with azulenes in the presence of strong acids other than perchloric acid. The chloride (I) was isolated in high yield when azulene and 1-formylazulene were heated in acetic acid or acetonitrile saturated with hydrogen chloride. The bromides (IV), (X), and (XIII) were similarly obtained in good yield when the appropriate azulenes and azulene aldehydes (see Table 2) in acetic acid or acetonitrile were treated with 50% (w/v) hydrogen bromide in acetic acid. 1-1′-Azulenylmethyleneazulenium iodides are conveniently prepared by addition of an excess of sodium iodide to boiling solutions of the corresponding chlorides or bromides. Unexpectedly, the product thus obtained from guaiazulene and 1-formyl-3-methylazulene gave analytical data corresponding to $C_{27}H_{27}I_2$, in place of the expected $C_{27}H_{27}I$, and is probably a lattice compound containing iodide and periodide ions in equal proportions. The bromides are more stable than the chlorides; they are comparable to the corresponding perchlorates and iodides in stability and solubility in organic solvents but are much more soluble in water.

The reaction of azulenes with ethyl orthoformate in the presence of strong acids was investigated as a possible general method of synthesis of symmetrical 1-1′-azulenylmethyleneazulenium salts. This reaction was first described briefly by Aldanowa and Stepanow [3] who used it to prepare the dye salts (I) and (II). We have confirmed these results but find further that the type of product depends upon the degree of alkylation of the azulene. Azulene and 1-methylazulene with either stoicheiometric quantities or an excess of ethyl orthoformate in the presence of perchloric acid gave almost quantitative yields of the salts (II) and (V), respectively. In contrast, perchloric acid, guaiazulene, and a large excess (800%) of ethyl orthoformate in ethanol gave a 90% yield of 3-ethoxymethyleneguaiazulenium perchlorate (XXI). 4,6,8-Trimethylazulene likewise gave 1-ethoxymethylene-4,6,8-trimethylazulenium perchlorate (XVIII) in 94% yield.* Other conditions remaining the same, the proportion of ethyl orthoformate determines the yield of substituted 1-ethoxymethyleneazulenium perchlorate. Results of experiments in which the excess of ethyl orthoformate was varied are tabulated.

Azulene (A)	% Excess of $HC(OEt)_3$ (B)	Molar ratio B/A	Yield (%)
Guaiazulene	100	2 : 1	0
,,	400	5 : 1	55
,,	800	9 : 1	90
4,6,8-Trimethylazulene	620	7·2 : 1	5
,, ,,	800	9 : 1	94

3-Ethoxymethyleneguaiazulenium and 1-ethoxymethylene-4,6,8,-trimethylazulenium perchlorate react at once with azulenes in alcohols or acetonitrile to form 1-1′-azulenylmethyleneazulenium perchlorates. No appreciable reaction takes place, however, in the presence of perchloric acid. Such salts [(VI)—(IX) and (XIV)] as could not be prepared by the condensation of 1-formylazulenes with azulenes in the presence of perchloric acid were obtained by this method. Since the azulenes whose 1-aldehydes fail to condense with azulenes in the presence of perchloric acid are those which form isolable 1-ethoxymethyleneazulenium perchlorates, the two limited methods of preparation together constitute one general synthetic method.

* Hitherto only one compound of this type has been described,[4] namely, the corresponding fluoroborate, which was formed in the reaction of triethyloxonium fluoroborate with 1-formyl-4,6,8-trimethylazulene.

[3] Aldanowa and Stepanow, *Zhur. obshchei Khim.*, 1959, **29**, 339 (*Chem. Abs.*, 1960, **54**, 462).
[4] Hafner and Bernhard, *Annalen*, 1959, **625**, 108.

The difference in behaviour of azulenes depends upon their degree of alkylation. Electron-release by the alkyl substituents reduces the electrophilic character of the methine carbon atom of 1-ethoxymethyleneazulenium salts. Thus, while 1-ethoxymethyleneazulenium perchlorate (XV) cannot be isolated but condenses at once with unchanged azulene to form the dye salt (II), 3-ethoxymethyleneguaiazulenium perchlorate (XXI) cannot further react and is itself the reaction product.

The capability of azulenes to condense with substituted 1-ethoxymethyleneazulenium perchlorates, immediately in the absence of, but to a negligible extent in the presence of an excess of perchloric acid, must be attributed to their conversion under the latter conditions into the unreactive azulenium cations. Connected with this is the dependence of the yield of alkyl-substituted ethoxymethyleneazulenium perchlorates upon the magnitude of the excess of ethyl orthoformate. This is believed to depend upon the action of the orthoester which makes available the azulene from its unreactive cation.

Guaiazulene and 4,6,8-trimethylazulene also condensed with ethyl orthoformate in the presence of 50% (w/v) hydrogen bromide in acetic acid to give the bromides (XIX) and (XVI), respectively, which are very soluble in polar organic solvents and are sensitive to atmospheric moisture. The latter salt alone could be isolated pure. When sodium iodide was present the considerably more stable and much less soluble 3-ethoxymethyleneguaiazulenium iodide (XX) and 1-ethoxymethylene-4,6,8-trimethylazulenium iodide (XVII) were obtained. These salts condense readily with azulenes to form 1-1′-azulenylmethyleneazulenium halides; *e.g.*, (XX) with azulene gives 1-1′-azulenylmethylene-5-isopropyl-3,8-dimethylazulenium iodide (XI).

1-Ethoxymethyleneazulenium salts are readily hydrolysed by water to the corresponding aldehydes, thus providing the most convenient syntheses of 1-formylazulenes. 3-Formylguaiazulene and 1-formyl-4,6,8-trimethylazulene were obtained in 89 and 92% yields through the perchlorates (XXI) and (XVIII).

In a further synthesis of symmetrical 1-1′-azulenylmethyleneazulenium salts, azulenes were treated with chloromethoxymethane and perchloric acid in methanol. Guaiazulene gave 5-isopropyl-1-(5-isopropyl-3,8-dimethyl-1-azulenylmethylene)-3,8-dimethylazulenium perchlorate (XIV), but the yield was poor, and attempts to improve and extend the method gave unpromising results.

The visible absorption spectra of all 1-1′-azulenylmethyleneazulenium salts examined consist of a single, sharp, intense absorption band and are exemplified by those of the perchlorates (II) and (XII).[2] Table 1 records the position and intensity of this band for sixteen salts. The position of $\lambda_{max.}$ for a series of salts containing the same cation, *e.g.*, (X), (XI), and (XII) [compounds 6—8 (Table 1)] is unaffected by the nature of the anion, except in the series of the 5-isopropyl-3,8-dimethyl-1-(3-methyl-1-azulenylmethylene)azulenium salts [compounds 13—15 (Table 1)] in which the complex iodide $C_{27}H_{27}I_2$ shows a small hypsochromic displacement (2 mμ) relative to the normal bromide or perchlorate. The following observations on the perchlorates are noteworthy. (*a*) Alkylation of one or both azulene nuclei always produces a bathochromic displacement of $\lambda_{max.}$ whose magnitude depends upon the position(s) and number of substituents. (*b*) For any series of 1-1′-azulenylmethyleneazulenium perchlorates ($\overset{+}{Y}$=CH–Z ⟷ Y–$\overset{+}{C}$H–Z ⟷ Y–CH=$\overset{-}{Z}$)ClO_4^- in which the nucleus Y is the same, $\lambda_{max.}$ shifts progressively to longer wavelength as Z changes in the order 1-(azulene), 1-(4,6,8-trimethylazulene), 1-(3-methylazulene), 3-(guaiazulene) [1-(5-isopropyl-3,8-dimethylazulene)]. (*c*) Definite shifts can be associated with a substituent, or group of substituents, as follows: 4,6,8-trimethyl, +9; 3-methyl, +16; 5-isopropyl-3,8-dimethyl, +26; 5-isopropyl-8-methyl, +10 mμ (calc. by difference of the immediately preceding two groups). (*d*) The shifts are additive. Agreement between calculated and observed values of $\lambda_{max.}$ is good in the case of most salts [*e.g.*, 1′-Me + 4-Me + 6-Me + 8-Me, +25 mμ; obs. for (VII), +26 mμ]. Exceptionally, in the case of the symmetrically alkylated dyes, observed values of $\Delta\lambda_{max.}$ are greater than

those calculated by the additivity rule [*e.g.*, 1-Me + 4-Me + 7-Pr^{i} + 1′-Me + 4′-Me + 7′-Pr^{i}, +52 mμ; obs. for (XIV), +62 mμ].

TABLE 1. *Visible absorption maxima* (mμ) *of* 1-1′-*azulenylmethyleneazulenium salts in acetic acid.*

No.		$\lambda_{max.}$	log ε
1	1-1′-Azulenylmethyleneazulenium chloride	618	[a]
2	,, ,, perchlorate	618 [b]	5·08
3	1-1′-Azulenylmethylene-4,6,8-trimethylazulenium perchlorate	627 [c]	5·00
4	1-1′-Azulenylmethylene-3-methylazulenium perchlorate	634	5·02
5	4,6,8-Trimethyl-1-(4,6,8-trimethyl-1-azulenylmethylene)azulenium perchlorate	640	4·94
6	1-1′-Azulenylmethylene-5-isopropyl-3,8-dimethylazulenium bromide	644	5·00
7	1-1′-Azulenylmethylene-5-isopropyl-3,8-dimethylazulenium iodide	644	4·96
8	1-1′-Azulenylmethylene-5-isopropyl-3,8-dimethylazulenium perchlorate	644 [d]	4·98
9	4,6,8-Trimethyl-1-(3-methyl-1-azulenylmethylene)azulenium perchlorate	644	5·03
10	3-Methyl-1-(3-methyl-1-azulenylmethylene)azulenium bromide	652	4·99
11	3-Methyl-1-(3-methyl-1-azulenylmethylene)azulenium perchlorate	652	5·01
12	5-Isopropyl-3,8-dimethyl-1-(4,6,8-trimethyl-1-azulenylmethylene)azulenium perchlorate	653	4·93
13	5-Isopropyl-3,8-dimethyl-1-(3-methyl-1-azulenylmethylene)azulenium iodide [e]	661	5·00
14	5-Isopropyl-3,8-dimethyl-1-(3-methyl-1-azulenylmethylene)azulenium bromide	663	4·94
15	5-Isopropyl-3,8-dimethyl-1-(3-methyl-1-azulenylmethylene)azulenium perchlorate	663	4·97
16	5-Isopropyl-1-(5-isopropyl-3,8-dimethyl-1-azulenylmethylene)-3,8-dimethylazulenium perchlorate	680	5·08

[a] Value uncertain owing to instability. [b] Kirby and Reid, *J.*, 1960, 494. [c] In 4% (v/v) acetonitrile in acetic acid. [d] Redetermined value; previously recorded value, 645 mμ. [e] Complex iodide $C_{27}H_{27}I_3$.

EXPERIMENTAL

M. p.s were determined on a Kofler heating stage which, unless otherwise stated, was preheated to *ca.* 5—10° below the recorded m. p. Specimens for analysis were dried for 6—10 hr. at *ca.* 85°/0·1 mm. Visible spectra were determined with a Unicam S.P. 600 instrument.

Materials.—Acetic acid was of " AnalaR " grade. Acetonitrile was purified by successive distillations from phosphoric anhydride and freshly dried potassium carbonate, then redistilled before use. Ethyl orthoformate was fractionally distilled before use. Light petroleum was of boiling range 40—60°. Hydrogen bromide in acetic refers to 50% (w/v) hydrogen bromide in acetic acid. Perchloric acid refers to 70—72% (w/w) perchloric acid of " AnalaR " grade.

Condensation (A) *of Azulenes with* 1-*Formylazulenes in the Presence of Acids.*—Condensations were by one of the following general procedures (for details see Table 2).

Procedure A1. Perchloric acid (0·4 ml.) was added to the azulenealdehyde (0·002 mole) and the azulene (0·0022 mole) in acetic acid (25 ml.), and the solution was boiled for 2 min. In most cases the product crystallised extensively from the boiling blue solution. It was filtered off from the cooled solution, washed with acetic acid followed by ether, and recrystallised.

Procedure A2. A saturated solution of hydrogen chloride in acetic acid (1 ml.) was added to the azulenealdehyde (0·002 mole) and the azulene (0·002 mole) dissolved in acetonitrile (10 ml.), and the solution was boiled for 2 min. The product was filtered off from the cooled solution, washed with acetonitrile followed by ether, and recrystallised.

Procedure A3. Hydrogen bromide in acetic acid (0·5 ml.) was added to the azulenealdehyde (0·002 mole) and the azulene (0·002 mole) in boiling acetic acid (20 ml.), and the solution was boiled for 2 min. The filtered product was washed with acetic acid followed by much ether, and recrystallised.

Procedure A4. A saturated solution of hydrogen chloride in acetic acid (1 ml.) was added to the azulenealdehyde (0·002 mole) and the azulene (0·002 mole) in acetic acid (10 ml.). The solution was boiled for 1 min. Anhydrous sodium iodide (600 mg., 0·004 mole) was washed into the solution with acetic acid (10 ml.), and the resulting mixture was boiled for a further 2 min. In all cases the iodide partly crystallised from the boiling solution. It was filtered off from the cooled solution, washed successively with water, acetic acid, and ether, and recrystallised.

Condensation (B) *of Azulenes with* 1-*Ethoxymethyleneazulenium Salts.*—Condensations were by one of the following general procedures (for details see Table 2).

Procedure B1. A mixture of the azulene (0·002 mole), the 1-ethoxymethyleneazulenium

salt (0·002 mole), and methanol (12 ml.) was boiled for 2 min., then allowed to cool slowly to room temperature. The product was washed with a small volume of methanol and recrystallised from a suitable solvent.

TABLE 2. *Preparation of* 1-1′*-azulenylmethyleneazulenium salts; condensation of azulenes with* (A) 1*-formylazulenes and strong acids,* (B) 1*-ethoxymethyleneazulenium salts.*

Procedure	Azulene	1-Formylazulene or 1-ethoxymethylene azulenium salt	Product no.	Yield (%)	Colour †	Solvent	M. p. *
A2	Unsubst.	1-Formylazulene	1	82	Black [a]	[b]	[c]
A1	,,	1-Formylazulene	2 [d]	100	Black	N	>350° [e]
B3	,,	1-Ethoxymethylene-4,6,8-trimethylazulenium perchlorate	3	50	Black	N	>270° [f]
A1	,,	1-Formyl-3-methylazulene	4	100	Black [h]	N	350 [ft]
A1	1-Methyl	1-Formylazulene	4	97	Black [h]	N	350 [ft]
B2	4,6,8-Trimethyl	1-Ethoxymethylene-4,6,8-trimethylazulenium perchlorate	5	20	Black	M	>300 *
A3	Guaiazulene	1-Formylazulene	6	92	Green	C	188° [j]
B1	Unsubst.	3-Ethoxymethyleneguaiazulenium iodide	7	47	Violet-black	M2N	180—181·5
A1	Guaiazulene	1-Formylazulene	8 [d]	85	Green	N	199—200·5
B1	1-Methyl	1-Ethoxymethylene-4,6,8-trimethylazulenium perchlorate	9	65	Black	N	274—280 [k]
A3	1-Methyl	1-Formyl-3-methylazulene	10	92	Green [l]	N	280 [km]
A1	1-Methyl	1-Formyl-3-methylazulene	11	100	Green	N	350 [ft]
B2	Guaiazulene	1-Ethoxymethylene-4,6,8-trimethylazulenium perchlorate	12	20	Blue	M	217—219
A4	Guaiazulene	1-Formyl-3-methylazulene	13	55	Black	N	214 [n]
A3	Guaiazulene	1-Formyl-3-methylazulene	14	75	Green	C2N	185—187
A1	Guaiazulene	1-Formyl-3-methylazulene	15	84	Green	C	>265 *
B1 [o]	Guaiazulene	3-Ethoxymethyleneguaiazulenium perchlorate	16	3	Black	C	247—250 *

	Found (%)				Required (%)		
No.	C	H	Hal	Formula	C	H	Hal
1 [p]	85·6	5·6		$C_{21}H_{15}Cl$	83·3	5·0	
2 [d]	68·5	4·0	9·1	$C_{21}H_{15}ClO_4$	68·8	4·1	9·7
3	69·8	5·7	8·8	$C_{24}H_{21}ClO_4$	70·5	5·2	8·7
4	69·8	4·4	9·1	$C_{22}H_{17}ClO_4$	69·4	4·5	9·3
5	72·2	6·2	8·5	$C_{27}H_{27}ClO_4$	71·9	6·0	7·9
6	73·3	6·4		$C_{26}H_{25}Br$	74·8	6·0	
7	67·4	5·5		$C_{26}H_{25}I$	67·3	5·4	
8 [d]	71·1	5·6	8·2	$C_{26}H_{25}ClO_4$	71·5	5·8	8·1
9	71·3	5·9	8·2	$C_{25}H_{23}ClO_4$	71·0	5·5	8·4
10	73·5	5·5	21·2	$C_{23}H_{19}Br$	73·6	5·1	21·3
11	70·6	5·1	9·5	$C_{23}H_{19}ClO_4$	70·0	4·9	9·0
12	72·1	6·7	7·3	$C_{29}H_{31}ClO_4$	72·8	6·5	7·4
13	54·8	4·6	41·7	$C_{27}H_{27}I_2$	53·6	4·5	41·9
14	74·9	6·4		$C_{27}H_{27}Br$	75·2	6·3	
15	71·5	5·9	8·5	$C_{27}H_{27}ClO_4$	71·9	6·0	7·9
16	73·3	7·1	6·9	$C_{31}H_{25}ClO_4$	73·4	7·0	7·0

* With decomp. † Needles unless otherwise stated.

Recrystn. solvents: C = acetic acid. M = methanol. N = acetonitrile. C2N = acetic acid (once), then from acetonitrile (twice). M2N = methanol (once), then from acetonitrile (twice).

[a] Powder. [b] Decomp. during attempted recrystn. from acetonitrile. [c] Does not melt <340°. [d] Kirby and Reid, *J.*, 1960, 494. [e] Decomp. without melting. [f] Block preheated to ≮350. [ft] Block heated from room temperature. [h] Green reflex. [i] Explodes. [j] Block preheated to ≮188°. [k] Decomp. with partial melting. [l] Prisms. [m] Block preheated to ≮280°. [n] Block preheated to ≮214°. [o] Reaction solution diluted with dry ether (3 ml.), then set aside for 3 hr. [p] No satisfactory analysis.

Procedures B2 *and* B3. These were identical with the preceding except that the volumes of methanol used were, respectively, 20 and 30 ml.

Condensation of Ethyl Orthoformate with Azulenes and Strong Acids.—(a) *With azulene and perchloric acid.* Perchloric acid (2·5 ml.) in ethanol (15 ml.) at room temperature was added to a solution of azulene (1·28 g., 0·01 mole) and ethyl orthoformate (15 ml., 0·09 mole) in ethanol (30 ml.), also at room temperature. 1-1′-Azulenylmethyleneazulenium perchlorate (II) (1·80 g., 98%) separated at once from the resulting blue solution as black needles, identical spectrally

and in physical properties with the product from azulene, 1-formylazulene, and perchloric acid.[2] The formation of 1-ethoxymethyleneazulenium perchlorate (XV) could not be detected.

(b) *With 1-methylazulene and perchloric acid.* The condensation was carried out as described for the preceding experiment, but with 1-methylazulene (1·42 g., 0·01 mole) in place of azulene. Recrystallisation of the product (3·83 g., 97%) from acetonitrile gave 3-methyl-1-(3-methyl-1-azulenylmethylene)azulenium perchlorate (V), identical (m. p. and visible spectrum) with the product of condensation of 1-methylazulene, 1-formyl-3-methylazulene, and perchloric acid. No trace of 1-ethoxymethylene-3-methylazulenium perchlorate was detected.

(c) *With guaiazulene and perchloric acid.* Perchloric acid (2·5 ml., 0·03 mole, 200% excess) in dry ethanol (15 ml.) at room temperature was added all at once to a solution of guaiazulene (1·98 g., 0·01 mole) and ethyl orthoformate (15 ml., 0·09 mole, 800% excess) in dry ethanol (30 ml.), also at room temperature. Orange-yellow plates began to separate almost immediately in the orange-yellow solution. After 5 min. dry ether (15 ml.) was added with swirling to complete the crystallisation. The filtered product (3·23 g., 90%) was washed with anhydrous ethanol (15 ml.), followed by dry ether (100 ml.), and was thus satisfactory for further reactions. For analysis a specimen was dissolved in the minimum volume of boiling acetone and an equal volume of dry ether was subsequently added. *3-Ethoxymethyleneguaiazulenium perchlorate* (XXI) crystallised as orange needles which became green > 155° and melted at 161—163° (decomp.) (Found: C, 60·9; H, 6·9; Cl, 10·4. $C_{15}H_{23}ClO_5$ requires C, 60·9; H, 6·5; Cl, 10·0%). When the quantity of ethyl orthoformate was 8·3 ml. (0·05 mole, 400% excess) the yield fell to 1·960 g. (55%); the use of 3·32 ml. (0·02 mole, 100% excess) gave no crystalline product at all. Attempts to prepare the symmetrical dye salt (XIV) by the condensation of guaiazulene with a stoicheiometric amount or with a large excess of ethyl orthoformate in the presence of perchloric acid, either in boiling solution or at room temperature, were unsuccessful.

(d) *With 4,6,8-trimethylazulene and perchloric acid.* (i) The condensation was carried out as in (c), with 4,6,8-trimethylazulene (1·70 g., 0·01 mole) in place of guaiazulene. *1-Ethoxymethylene-4,6,8-trimethylazulenium perchlorate* (XVIII) (3·05 g., 94%) crystallised at once as greenish-yellow needles, unchanged in form after recrystallisation from acetonitrile. It does not melt but slowly becomes grey and finally black above 180° without losing shape (Found: C, 58·8; H, 6·1; Cl, 10·8. $C_{16}H_{19}ClO_5$ requires C, 58·8; H, 5·9; Cl, 10·9%).

(ii) The condensation was repeated with 4,6,8-trimethylazulene (3·40 g., 0·02 mole), ethyl orthoformate (24 ml., 0·144 mole, 620% excess), perchloric acid (5 ml., 0·06 mole, 200% excess), and absolute ethanol (90 ml.). The mixture became bluish-purple and a small quantity of solid separated. The mixture was hydrolysed with water (1 l.) and extracted exhaustively with ether. The ether extract was worked up in the usual manner, and the residue obtained on evaporation of solvent was dissolved in light petroleum for chromatography on alumina. Elution with light petroleum gave 4,6,8-trimethylazulene (2·99 g., 88% recovery). Subsequent elution with ether gave 1-formyl-4,6,8-trimethylazulene (196 mg., corresponding to 5% conversion of 4,6,8-trimethylazulene into 1-ethoxymethylene-4,6,8-trimethylazulenium perchlorate).

Attempts to prepare the symmetrical dye (VIII) by condensing 4,6,8-trimethylazulene with ethyl orthoformate in the presence of perchloric acid were unsuccessful.

(e) *With 4,6,8-trimethylazulene and hydrogen bromide.* Hydrogen bromide in acetic acid (0·5 ml.), dissolved in dry ethanol (3 ml.), was added to a solution of 4,6,8-trimethylazulene (340 mg., 0·002 mole), ethyl orthoformate (5 ml., 0·03 mole, 1400% excess), and dry ethanol (3 ml.) at room temperature. *1-Ethoxymethylene-4,6,8-trimethylazulenium bromide* (XVI) (308 mg., 50%) crystallised at once from the green solution. It was filtered off, washed with ethanol followed by ether, and dried at 100° for 5 min. Work must be as rapid as possible since hydrolysis occurs in air, especially in the presence of solvents. Recrystallisation from acetonitrile gave green prisms, m. p. 146—150° (decomp.) (Found: C, 62·1; H, 5·7. $C_{16}H_{19}BrO$ requires C, 62·55; H, 6·2%).

3-Ethoxymethyleneguaiazulenium Iodide.—Hydrogen bromide in acetic acid (4 ml.), dissolved in dry ethanol (30 ml.) at room temperature, was added to a solution of guaiazulene (4 g., 0·02 mole), anhydrous sodium iodide (6 g., 0·04 mole), ethyl orthoformate (30 ml.), and dry ethanol (30 ml.), also at room temperature. *3-Ethoxymethyleneguaiazulenium iodide* (XX) (6·16 g., 81%) crystallised at once as garnet-red needles which were washed with ethanol, followed by ether, and dried *in vacuo* (Found: C, 55·8; H, 6·1; I, 31·8. $C_{16}H_{23}IO$ requires C, 56·6; H, 6·1; I, 33·2%). The salt, when freshly prepared, has m. p. 128—130° (decomp. to black liquid), but slowly changes at room temperature into orange-brown needles which decompose slowly

XUM

with partial melting >135° and melt completely to a green liquid at 152°. The change is accelerated by heat and occurs during recrystallisation from acetonitrile.

1-Ethoxymethylene-4,6,8-trimethylazulenium Iodide.—Hydrogen bromide in acetic acid (0·5 ml.), when dissolved in dry ethanol (4 ml.) and added to a cold solution of 4,6,8-trimethylazulene (340 mg., 0·002 mole), ethyl orthoformate (5 ml., 0·03 mole), and anhydrous sodium iodide (700 mg.) in dry ethanol (10 ml.), gave directly 1-ethoxymethylene-4,6,8-trimethylazulenium iodide (XVII) (700 mg., 100%), brown needles, m. p. 145—150° (decomp.), which was analysed without recrystallisation owing to decomposition in hot solvents (Found: C, 53·3; H, 5·3. Calc. for $C_{16}H_{19}IO$: C, 54·3; H, 5·4%).

Hydrolysis of 1-Ethoxymethyleneazulenium Salts.—*3-Ethoxymethyleneguaiazulenium perchlorate.* Cold water (100 ml.) was added slowly with swirling to an initially boiling solution of 3-ethoxymethyleneguaiazulenium perchlorate (2·84 g.) in acetone (30 ml.). 3-Formylguaiazulene crystallised at once as brown needles (1·795 g., 99%), identical in m. p. and mixed m. p. with an authentic specimen.

1-Ethoxymethylene-4,6,8-trimethylazulenium perchlorate. This salt (3·05 g.), acetone (200 ml.), and water (200 ml.) were shaken together for several minutes, or until hydrolysis was complete. The mixture was diluted with water and extracted with ether (2 × 350 ml.), and the combined extracts were worked up in the usual manner. Evaporation left 1-formyl-4,6,8-trimethylazulene (1·83 g., 99%) which after one recrystallisation from ethanol had m. p. 105—106° (lit.,[4] m. p. 106—107°).

Condensation of Guaiazulene, Chloromethoxymethane, and Perchloric Acid.—Guaiazulene (2400 mg.), chloromethoxymethane (245 mg.), and anhydrous ethanol (10 ml.) were heated to the b. p., perchloric acid (1·5 ml.) was added, and the solution was boiled for 30 sec. Dry ether (5 ml.) was added with swirling to the cooled solution which was then left at room temperature for 1·5 hr. 5-Isopropyl-1-(5-isopropyl-3,8-dimethyl-1-azulenylmethylene)3,8 dimethylazulenium perchlorate (XIV) (75 mg., 5%) crystallised as flat, black needles which, after one recrystallisation from acetic acid, was identical (m. p., mixed m. p., and visible spectrum) with the product of condensation of guaiazulene with 3-ethoxymethyleneguaiazulenium perchlorate. Addition of dry ether (20 ml.) to the filtrate afforded a further 80 mg. of slightly less pure material, bringing the total yield to 155 mg. (10%).

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336. *The Interaction of Phosphorus Pentachloride with Tertiary Amines.*

By I. R. Beattie and M. Webster.

Contrary to previous work it has been shown that phosphorus pentachloride and pyridine react to form a 1 : 1 addition compound. The reaction of phosphorus pentachloride with trimethylamine has been re-examined and shown to result in the formation of triethylammonium chloride, previously formulated as an addition compound of chlorine and the amine.

The donor properties of phosphorus pentachloride with Lewis acids, such as tin tetrachloride and aluminium trichloride, are well established.[1] Conversely, the hexachlorophosphate anion must be regarded as the only established example of the phosphorus pentachloride molecule's acting as an acceptor. This ion is present in solid phosphorus pentachloride,[2] and Gutmann and Mairinger [3] report the formation of crystalline tetraethylammonium hexachlorophosphate. The mechanisms suggested for some reactions of

[1] See, *e.g.*, Abegg's "Handbuch der Anorganischen Chemie," Leipzig, 1907, III, **3**, 415; Groenveld, *Rec. Trav. chim.*, 1952, **71**, 594; Groenveld and Zuur, *ibid.*, 1953, **72**, 617.
[2] Clark and Powell and (independently) A. F. Wells, *J.*, 1942, 642.
[3] Gutmann and Mairinger, *Z. anorg. Chem.*, 1957, **289**, 279.

Vol. 1961, page 1730, line 9 *. *For* trimethylamine *read* triethylamine.

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phosphorus pentachloride [4] formally involve the tetrachlorophosphorus(v) cation as an acceptor group. However, these species have not been isolated as true intermediates. In view of the stability of compounds such as the 2 : 1 addition compound of pyridine with silicon tetrachloride [5] and the 1 : 1 addition compound of pyridine with phosphorus pentafluoride,[6] we reinvestigated the reaction between phosphorus pentachloride and pyridine.

Work by Sell and Dootson [7] indicates that phosphorus pentachloride dissolved in phosphorus oxychloride does not react with pyridine, although it appears that their method of study would not have shown the presence of addition compounds. More recently Hutton and Webb [8] reported that the gradual addition of phosphorus pentachloride to dry pyridine gave an initial precipitate of pyridinium chloride. On further addition of phosphorus pentachloride a very hygroscopic solid was formed which the authors formulated as (I) although they did not indicate the source of the hydrogen chloride. An obvious criticism of this work, in which the reagents were directly mixed, lies in the difficulty of studying a reaction between a solid and a liquid to give a solid product.

(I) $C_5H_5N \rightarrow Cl$ / $(PCl_3)\cdot H\cdot C_5H_5N$

We find that phosphorus pentachloride and pyridine react to give a 1 : 1 addition compound. The approximate stoicheiometry has been found by adding successive amounts of pyridine to phosphorus pentachloride in a vacuum system, while measuring the vapour pressure in the system after each addition. The results are shown in Fig. 1. The scatter towards the pyridine-rich end of the system is presumably due to incomplete reaction. These results point to the formation of a 1 : 1 addition compound of reasonable stability. Verification of this ratio was obtained by titrating pyridine with a solution of phosphorus pentachloride in carbon disulphide, the end-point being indicated by lack of further precipitation on addition of pyridine. The ratio found in this way was PCl_5 : py = 1 : 0·97. The solid product was removed by centrifugation, and completely analysed after excess of pyridine and carbon disulphide had been pumped away. The addition product sublimed readily *in vacuo*, and was hydrolysed rapidly and completely to phosphate, chloride, and pyridine.

These results suggest that phosphorus pentachloride can act as an acceptor. This seems to be at variance with some conclusions on the interaction of trimethylamine and triethylamine with phosphorus pentachloride in a vacuum system. Holmes and Bertaut [9] report that phosphorus trichloride is the volatile product of this reaction, while they formulate the solid products as $(Me_3N)_2,Cl_2$ and Et_3N,Cl_2 in each case. Their reaction scheme could thus be written

$$PCl_5 \rightleftharpoons PCl_3 + Cl_2 \quad \ldots \quad (1)$$

$$Cl_2 + 2Me_3N \longrightarrow (Me_3N)_2,Cl_2 \quad \ldots \quad (2)$$

and

$$Cl_2 + Et_3N \longrightarrow Et_3N,Cl_2 \quad \ldots \quad (3)$$

This does not agree with our results. Further, Hantzsch and Graf [10] state that " dichlorides of the form R_3N,Cl_2 are as yet scarcely known " and add that the addition compound of trimethylamine and chlorine is exceedingly unstable. This has been confirmed by Böhme and Krause.[11] The compound $(Me_3N)_2,Cl_2$ is not reported in the literature except as a private communication from an unnamed investigator.[9] Examination of Holmes and Bertaut's results shows that the stoicheiometry required by equations (1), (2), and (3) is not exactly obeyed. The solid products of reaction might well by formulated as amine

[4] Newman and Wood, *J. Amer. Chem. Soc.*, 1959, **81**, 4300.
[5] Hulme, Leigh, and Beattie, *J.*, 1960, 366, and references therein.
[6] Woolf, *J. Inorg. Nuclear Chem.*, 1956, **3**, 285.
[7] Sell and Dootson, *J.*, 1898, **73**, 432.
[8] Hutton and Webb, *J.*, 1931, 1518.
[9] Holmes and Bertaut, *J. Amer. Chem. Soc.*, 1958, **80**, 2980.
[10] Hantzsch and Graf, *Ber.*, 1905, **38**, 2154.
[11] Böhme and Krause, *Ber.*, 1951, **84**, 170.

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hydrochlorides. We reinvestigated the interaction of triethylamine with phosphorus pentachloride, to determine whether the initial stage involved dehydrogenation of the amine.

On rapid addition of an excess of triethylamine to a solution of phosphorus pentachloride in carbon disulphide, a white precipitate, almost exclusively of triethylammonium chloride was formed immediately (mixed m. p. and infrared spectra). The interaction of phosphorus pentachloride with triethylamine thus results in dehydrogenation of the amine. A test for diethylvinylamine with 2,5-dichloro-3,6-dimethoxy-*p*-benzoquinone [12] was negative.

The reduction of active metal halides with trialkylamines has been observed with titanium tetrachloride [13] and vanadium tetrachloride.[14] Further, our results do not conflict with the available experimental results of Holmes and Bertaut.

FIG. 1. *Vapour pressure–composition diagram for the addition of pyridine to phosphorus pentachloride.*

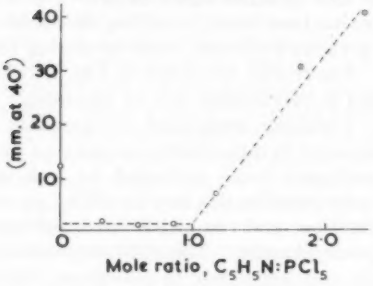
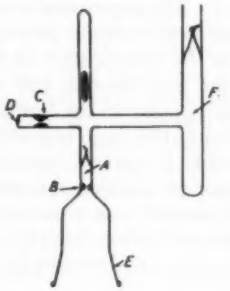


FIG. 2. *Apparatus used in the hydrolysis of the* 1 : 1 *addition compound of pyridine and phosphorus pentachloride.*



Experimental.—All work was carried out either in a vacuum system (complete absence of grease) or in a dry-box under nitrogen.

Reagents. Triethylamine. We were not able to remove the primary and secondary amines by the method suggested by Holmes and Bertaut.[9] Primary and secondary amines were removed by using benzenesulphonyl chloride followed by fractional distillation. The primary and secondary amines then totalled less than 0·05% of the product. The triethylamine was dried (CaH_2) and distilled *in vacuo* into ampoules which were then sealed. Carbon disulphide. This was dried over calcium hydride and distilled. Phosphorus pentachloride. This was sublimed *in vacuo* into ampoules which were then sealed.

Analysis of the complex. The 1 : 1 compound of phosphorus pentachloride and pyridine reacted violently with water so that hydrolysis was carried out in a sealed system (Fig. 2). The sample was introduced into *A* in a dry-box and the vessel was then stoppered. The apparatus was taken from the dry-box, the stopper removed, and the sample pumped out by rapidly connecting *E* to a ground-joint on the vacuum system. Water was introduced into *F*, and the apparatus joined to the vacuum system at *D*. After outgassing of the water, constriction *C* was sealed, and similarly after outgassing of the solid, constriction *B* was sealed. The thin glass septum separating *A* and *F* was broken to allow the sample to hydrolyse by carefully tipping it from *A* into the water in *F*. After hydrolysis the solution was transferred to a standard flask and made up to be about 0·2N with respect to nitric acid. Chloride was determined gravimetrically as silver chloride, phosphorus by precipitation as phosphomolybdate with ignition to P_2O_5,24MoO_3, and pyridine spectrometrically (Unicam S.P. 500; 255 mμ) as the pyridinium ion after removal of interfering anions by means of an ion-exchange resin

[12] Buckley, Dunstan, and Henbest, *J.*, 1957, 4901.
[13] Antler and Laubengayer, *J. Amer. Chem. Soc.*, 1955, **77**, 5250.
[14] Fowles and Pleass, *J.*, 1957, 1674.

in the chloride form. The spectrometer was previously calibrated by using known pyridine solutions containing chloride.

Results. Found: Cl, 61·5$_1$, 61·6$_7$; C_5H_5N, 27·7$_4$; P, 10·8$_1$, 10·7$_7$. Calc. for PCl_5,C_5H_5N: Cl, 61·7; C_5H_5N, 27·5; P, 10·8%.

Reaction of triethylamine with phosphorus pentachloride (quantities are approximate). Phosphorus pentachloride (10 mmoles) was dissolved in carbon disulphide (70 c.c.), and triethylamine (20 mmoles) was rapidly added dropwise; 7 mmoles of apparently pure triethylamine hydrochloride were precipitated during the addition of the amine. M. p.s (sealed tubes, uncorr.); triethylamine hydrochloride 253—254°; product 248—250°; mixed m. p. 251—252°.

The authors thank Dr. J. I. G. Cadogan for helpful discussion, Professor H. B. Henbest for a sample of 2,5-dichloro-3,6-dimethoxy-*p*-benzoquinone, the Royal Society for a grant for the purchase of a Unicam S.P. 500, and the D.S.I.R. for a grant (to M. W.).

KING'S COLLEGE, STRAND, W.C.2. [*Received, August 10th*, 1960.]

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337. *The Catalytic Action of Metal Alkyl–Metal Halide Complexes. Part I. The Dimerisation of* 1,1-*Diphenylethylene in Benzene–*n*-Butyl-lithium–Titanium Tetrachloride–Hydrogen Chloride Systems.*

By ALWYN G. EVANS and G. D. T. OWEN.

We have found that 1,1-diphenylethylene cannot be dimerised in LiBu–$TiCl_4$–benzene systems. The addition of hydrogen chloride, however, to such systems brings about a rapid dimerisation to the indane dimer. The effects of temperature, reagent concentration, and order of mixing on the rate of this dimerisation have been investigated.

THE dimerisation of 1,1-diphenylethylene by cationic catalysts has been studied previously.[1] We have now extended this work to metal alkyl–metal halide catalysts, using the system LiBu–$TiCl_4$–HCl–benzene. This work has been briefly described elsewhere [2] and we now give a detailed account of these reactions.

EXPERIMENTAL

(1) *Materials.*—Benzene,[3] titanium tetrachloride,[1] and hydrogen chloride [4] were prepared and purified as before under the most rigorous high-vacuum conditions. 1,1-Diphenylethylene was purified by distillation followed by treatment with stannic chloride,[3] and finally was distilled several times under high vacuum and stored under vacuum in ampoules.

n-Butyl-lithium was prepared by the action of lithium on n-butyl chloride in benzene.[5] We carried out the whole operation under high vacuum, using the apparatus shown in Fig. 1. Lithium wire (3 g.) was introduced into vessel *A* through a hole blown at *B*. The system was sealed off at *C*, and then evacuated. Tap *D* was closed, the vacuum seal to vessel *E*, which contained benzene, dried over potassium, was broken, and approximately 150 ml. of benzene were distilled on to the lithium in *A*, and the vessel sealed off at *F*. n-Butyl chloride (10 ml.), which had been purified by fractionation and high-vacuum distillation, was similarly introduced into *A* from vessel *G*, which was then sealed off at *H*. Immediately the n-butyl chloride was introduced a mildly exothermic reaction occurred, and tap *D* was opened periodically to pump evolved gas away. After about 1 hr., when the reaction had subsided and a purple solid had settled on the bottom of the vessel *A*, tap *D* was finally closed, and the mixture set aside overnight. The n-butyl-lithium solution was degassed before being sealed off from the high-vacuum

[1] Evans and E. D. Owen, *J.*, 1959, 4123, and earlier parts.
[2] Evans and G. D. Owen, (*a*) *Chem. and Ind.*, 1959, 1163; (*b*) *ibid.*, 1960, 47.
[3] Evans and Lewis, *J.*, 1957, 2975.
[4] Evans and Lewis, *J.*, 1959, 1946.
[5] Ziegler and Colonius, *Annalen*, 1930, **479**, 123.

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line at *I* and *J*. The solution was then filtered free from solid impurities through the sintered-glass disc *K* (No. 4 porosity) and collected in calibrated bulbs, *L*, and a storage vessel, *M*, which were then sealed off.

The concentration of n-butyl-lithium was estimated by the double titration method,[6a] high-vacuum techniques being used in the preparation of the solutions and in the reaction of butyl-lithium with benzyl chloride.[6b]

(2) *Kinetic Measurements.*—(a) *Normal method.* A solution of 1,1-diphenylethylene in benzene was introduced into dilatometers by the high-vacuum technique used earlier.[3] Known amounts of titanium tetrachloride, benzene solution of butyl-lithium, and hydrogen chloride, in that order (unless otherwise stated), were then added to the dilatometer by using the technique

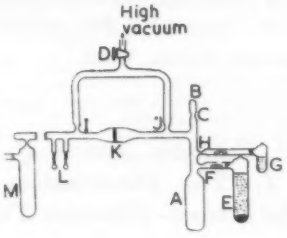
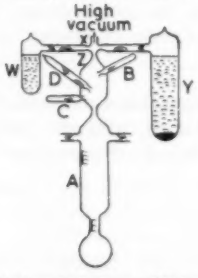


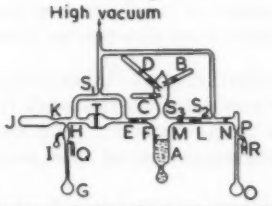
FIG. 1. *Apparatus for the preparation of n-butyl-lithium.*
(G) *Butyl chloride*; (E) *benzene.*

FIG. 2. *Apparatus for mixing monomer, benzene, titanium tetrachloride, butyl-lithium, and hydrogen chloride.*



(W) 1,1-*Diphenylethylene*; (Y) *benzene over sodium-potassium alloy*; (B) *titanium tetrachloride*; (C) *butyl-lithium*; (D) *hydrogen chloride.*

FIG. 3. *Apparatus for locating the catalytic activity.*



(A) *Benzene solution of* 1,1-*diphenylethylene*; (B) *titanium tetrachloride*; (C) *butyl-lithium*; (D) *hydrogen chloride*; (T) *sintered-glass diaphragm* (*No.* 4 *porosity*).

described earlier [1,4] for titanium tetrachloride and hydrogen chloride, the butyl-lithium solution being added in exactly the same way as for titanium tetrachloride. A brown precipitate formed which settled, leaving a clear supernatant liquor. The dilatometers were sealed off and placed in thermostats.

(b) *Method used to locate the catalytic activity.* By means of the apparatus shown in Fig. 2, a known volume of 1,1-diphenylethylene was distilled from *W* into the graduated vessel *A*, and the apparatus sealed at *X*. A known volume of benzene was distilled from *Y* into *A*, and the apparatus sealed off at *Z*. Vessel *A* was then attached to the system shown in Fig. 3 which was evacuated and sealed off at *S*1 and *S*2. The titanium tetrachloride (*B*), butyl-lithium solution (*C*), and hydrogen chloride (*D*) were introduced into the 1,1-diphenylethylene–benzene solution (*A*) in the usual way and the vessel was sealed off at S_3. A precipitate formed in *A*, and this and its supernatant liquor were then dealt with as follows.

A magnetic breaker *E* was used to break the vacuum seal *F*, and the apparatus tilted so as to filter the reacting system through the glass sinter *T* and into the dilatometer *G* which was

[6] (*a*) Gilman and Haubein, *J. Amer. Chem Soc.*, 1944, **66**, 1515; (*b*) Evans and George, unpublished work.

sealed off at *H*. The spectroscopic cell *I* was filled and sealed off, and the dilatometer finally placed in a thermostat. The rest of the filtrate passed into the tube *J* and was sealed off at *K*.

The magnetic breaker *L* was used to break the vacuum seals *M* and *N*. A benzene solution of 1,1-diphenylethylene, which had been previously placed in dilatometer *O*, was then poured through the apparatus, and the catalyst precipitate was washed back into the dilatometer which was sealed off at *P* and placed in a thermostat.

In this way we obtained two systems: that in dilatometer *G* contained the supernatant liquid and the original monomer, while that in dilatometer *O* contained the precipitate and fresh monomer solution.

(3) *Isolation and Identification of Reaction Products.*—The products were investigated by the method described earlier.[7]

(4) *The Reaction of Butyl-lithium with Titanium Tetrachloride.*—The [LiBu]/[$TiCl_4$] ratio below which free titanium tetrachloride is present in the supernatant liquid was studied by making use of the fact that free butyl-lithium in benzene is colourless, whereas free titanium tetrachloride in benzene is coloured owing to its complex with benzene,[1] which enables it to be detected down to concentrations of 2×10^{-4} mole $l.^{-1}$. Small amounts of titanium tetrachloride (of approx. 0·07 ml.), contained in small bulbs, were successively added under high vacuum to 40 ml. of a colourless solution containing $4{\cdot}18 \times 10^{-3}$ mole of butyl-lithium in benzene, the same technique being used as that for adding titanium tetrachloride to the reaction mixture. After each addition a brown precipitate formed which was allowed to settle; the supernatant liquid remained colourless for the first five additions, but the sixth gave an intensely yellow liquid showing the presence of free titanium tetrachloride in the benzene solution; 0·411 ml. of a benzene solution of butyl-lithium (0·60M) was then added to the system and the supernatant liquid became colourless. In this way the [LiBu]/[$TiCl_4$] ratio below which free titanium tetrachloride exists in the supernatant liquid was determined.

The [LiBu]/[$TiCl_4$] ratio above which free butyl-lithium is present in the supernatant liquid was investigated by making use of the fact that, although free butyl-lithium in benzene is colourless, yet in the presence of 1,1-diphenylethylene a coloured carbanion is formed.[8] This carbanion is yellow in dilute solution and deep cherry-red in concentrated solutions of 1,1-diphenylethylene. Benzene solutions which were molar in monomer and contained various amounts of titanium tetrachloride and butyl-lithium were made up as described in Experimental, Section 2 (a), and the colour of the supernatant liquid was observed for different [LiBu]/[$TiCl_4$] ratios. For this monomer concentration, free butyl-lithium can be detected by the carbanion colour down to concentrations of 10^{-5} mole $l.^{-1}$.[8] In this way, the [LiBu]/[$TiCl_4$] ratio above which free butyl-lithium exists in the supernatant liquid was determined.

Results

(1) *Products of Reaction.*—The final product of the reaction was analysed and it was found that the monomer was completely converted into the cyclic dimer 3-methyl-1,1,3-triphenylindane; no linear dimer, 1,1,3,3-tetraphenylbut-1-ene, could be detected even in the early stages of the reaction.

(2) *Rates of Dimerisation.*—(a) *Effect of hydrogen chloride.* The change in volume of the solution in the dilatometer was measured with time, and the initial rate determined. It was

Table 1.

Batch 1 Run No.	10^4 I.R.*	[M] (mole $l.^{-1}$)	10^3[LiBu] (mole $l.^{-1}$)	10^3[$TiCl_4$] (mole $l.^{-1}$)	10^3[HCl] (mole $l.^{-1}$)	Temp.
1	1·5	1·02	5·1	3·7	0	30·3°
2	62	1·02	5·1	3·7	5·8	30·3°
3	171	1·02	5·1	3·7	33	30·3°

* Initial rate, expressed in moles of dimer formed per l. per hr. M = the monomer, 1,1-diphenylethylene.

found that when the reagents were purified rigorously, a negligible reaction took place in the 1,1-diphenylethylene–titanium tetrachloride–butyl-lithium–benzene system [2b] (see Table 1 and Fig. 4). As the hydrogen chloride concentration was increased the rate increased.

[7] Evans, Jones, and Thomas, *J.*, 1957, 2095.
[8] Evans and George, *Proc. Chem. Soc.*, 1960, 144.

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(b) ***Temperature dependence.*** The effect of temperature is shown in Table 2 and the apparent activation energy was found to be $-11{\cdot}0 \pm 0{\cdot}3$ kcal. mole^{-1}.

(c) ***Reproducibility.*** Runs 1 and 4 (Table 2) were put on at the beginning and the end of the particular batch of runs. The reagent concentrations for them are identical, and it is seen that the rates are the same. This shows that, although the system is heterogeneous, comparison of rates within any one batch of experiments is justifiable. Our method was to allow the precipitate to settle and not to agitate the system.

TABLE 2.

Batch 2 Run No.	10^4 I.R.	[M] (mole l.$^{-1}$)	10^3[LiBu] (mole l.$^{-1}$)	10^3[$TiCl_4$] (mole l.$^{-1}$)	10^3[HCl] (mole l.$^{-1}$)	Temp.
1	15·0	0·94	4·8	3·7	0·99	30·3°
2	9·0	0·94	4·8	3·7	0·99	40·0
3	3·9	0·94	4·8	3·7	0·99	55·0
4	15·4	0·94	4·8	3·7	0·99	30·3

In view of the extreme sensitivity of the reaction to hydrogen chloride, we were not surprised to find that when we changed our batch of benzene we did not get exact reproducibility of rates although of course the general behaviour was the same from batch to batch.

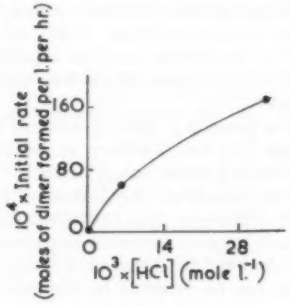

FIG. 4. *Effect of* [HCl] *on initial rate of dimerisation of* 1,1-*diphenylethylene in benzene at* 30·3°, *in the presence of titanium tetrachloride–butyl-lithium.*

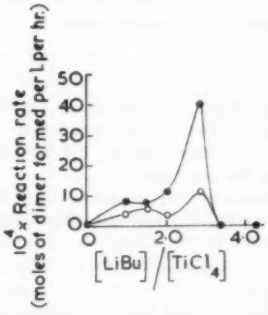

FIG. 5. *Effect of* [LiBu]/[$TiCl_4$] *ratio on the rate of dimerisation of* 1,1-*diphenylethylene.*
● *Initial rate*; ○ *rate at* 3% *dimerisation.*

(d) ***Effect of*** [LiBu]/[$TiCl_4$] ***ratio.*** The effect of the [LiBu]/[$TiCl_4$] ratio on the initial rate is shown in Table 3 and Fig. 5. It is seen that a sharp peak in the plot of initial rate against [LiBu]/[$TiCl_4$] occurs at a [LiBu]/[$TiCl_4$] ratio of 2·9. When the butyl-lithium concentration is in excess of this value the initial rate falls to zero, the solution in the dilatometer showing no contraction with time even after 14 days. The reaction rate falls off much faster than corresponds to disappearance of monomer, and suggests that the activity of the catalyst rapidly decreases as the reaction proceeds. The most marked decrease in rate occurs for the catalyst which is most active initially, *i.e.*, for a [LiBu]/[$TiCl_4$] ratio of 3. This effect is shown in Fig. 5.

(3) ***Reaction of Butyl-lithium with Titanium Tetrachloride.***—(a) ***The*** [LiBu]/[$TiCl_4$] ***ratio below which free titanium tetrachloride is present in the supernatant liquid.*** The tetrachloride was added

stepwise to a solution of butyl-lithium in benzene as described in Experimental, Section 4, and the results are given in sequence in Table 4 for the last two additions of titanium chloride and for the subsequent addition of butyl-lithium. It is found that excess of the tetrachloride is present in the supernatant liquid (shown by the yellow colour) when the [LiBu]/[$TiCl_4$] ratio is $\leqslant 1{\cdot}13$.

TABLE 3. *Experiments at 30·3° on the monomer–*LiBu–$TiCl_4$–HCl*–benzene systems, when* [M] $= 9{\cdot}6 \times 10^{-1}$ *mole l.*$^{-1}$ *and* [$TiCl_4$] $= 3{\cdot}7 \times 10^{-3}$ *mole l.*$^{-1}$.

Batch 3 Run No.	10^3[LiBu] (mole l.$^{-1}$)	$\frac{[LiBu]}{[TiCl_4]}$	Colour of supernatant liquid before addition of HCl	10^3[HCl] (mole l.$^{-1}$)	$10^4 \times$ I.R.
1	0	0	Yellow	1·07	0·3
2	3·5	0·95	Yellow	1·08	8·3
3	5·6	1·5	Colourless	1·07	7·1
4	7·5	2·0	Colourless	1·07	11·3
5	10·5	2·9	Colourless	1·07	40
6	12·6	3·4	Yellow	1·06	0
7	15·9	4·3	Deep yellow	1·07	0
8*	10·0	∞	Cherry-red	1·07	0

* $TiCl_4$ not present in this run.

TABLE 4.

10[LiBu] (mole l.$^{-1}$)	10^3[$TiCl_4$] (mole l.$^{-1}$)	$\frac{[LiBu]}{[TiCl_4]}$	Colour of supernatant liquid	10[LiBu] (mole l.$^{-1}$)	10^3[$TiCl_4$] (mole l.$^{-1}$)	$\frac{[LiBu]}{[TiCl_4]}$	Colour of supernant liquid
1·05	5·9	1·77	Colourless	1·05	9·3	1·13	Yellow
1·05	7·7	1·37	Colourless	1·11	9·3	1·19	Colourless

(b) *The* [LiBu]/[$TiCl_4$] *ratio above which free butyl-lithium is present in the supernatant liquid.* These observations were carried out on the reaction mixtures given in Table 3, and it is seen that excess of butyl-lithium (indicated by the coloured carbanion, see Experimental, Section 4) is present in the supernatant liquid for runs 6, 7, and 8, *i.e.*, when the [LiBu]/[$TiCl_4$] ratio is $\geqslant 3{\cdot}4$. The yellow colour of the supernatant liquid in runs 1 and 2 ([LiBu]/[$TiCl_4$] ratio $< 1{\cdot}13$) is due, of course, to excess of the tetrachloride (see above).

(4) *Location of Catalytic Activity.*—It was found that the solution in dilatometer *G* (see Experimental, Section 2b), containing the supernatant liquid and the original monomer, did not contract. To test whether this was due to the fact that all the monomer had been completely converted into dimer during the time of filtration (1 hr.), titanium tetrachloride was added to this dilatometer under high-vacuum conditions by using the vacuum seal *Q* (Fig. 3). The system immediately began to contract and gave a volume change equal to that expected for the conversion of 25% of the original monomer into the indane dimer. The dilatometer was then opened and the products were analysed. It was found that all the monomer had been converted into the indane dimer. This means that about 75% of the original monomer had dimerised before filtration was complete, but that the removal of the precipitate had stopped further reaction; the subsequent addition of titanium tetrachloride to the supernatant liquid had then brought about the titanium tetrachloride–hydrogen chloride-catalysed homogeneous dimerisation of the remaining 25% of monomer. The presence of monomer in the supernatant liquid after filtration was also confirmed (Experimental, Section 3) by analysis of that portion of the filtrate which was collected in the tube *J* (Fig. 3).

The precipitate, which was washed back into the dilatometer *O* (Fig. 3) with fresh monomer solution, showed catalytic activity in that the dilatometer solution contracted with time at an appreciable rate: 10% reaction to dimer in 19 hr. Analysis of the product showed it to be cyclic dimer.

(5) *Effect of using Large Concentrations of Butyl-lithium and Titanium Tetrachloride.*—After a dilatometer had been filled with a solution of 1,1-diphenylethylene (0·96 mole l.$^{-1}$), the alkyl (0·22 mole l.$^{-1}$), and the chloride (0·14 mole l.$^{-1}$), a negligible contraction was observed during a week and analysis of the solution showed that no dimerisation had occurred even at these high concentrations of alkyl and tetrachloride in the absence of hydrogen chloride.

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Discussion

Heterogeneity of Reaction.—The results show that the butyl-lithium–titanium tetrachloride–benzene system will not act as a catalyst for the dimerisation of 1,1-diphenylethylene, but that the addition of hydrogen chloride to such systems causes formation of the cyclic dimer. That this reaction does not occur in the homogeneous phase is shown by the following considerations: (*a*) It cannot be due to the titanium tetrachloride–hydrogen chloride homogeneous reaction since it occurs in systems for which the tetrachloride has been removed from the supernatant liquid by the alkyl, *i.e.*, systems for which the [LiBu]/[$TiCl_4$] ratio is $\geqslant 1{\cdot}19$ [see Results, Section 3 (a)]. Indeed, even if all the original tetrachloride were present in the liquid phase, the reaction rates would be some 25 times faster than could be expected for the titanium tetrachloride–hydrogen chloride homogeneous reaction. (*b*) This reaction is not due to any butyl-lithium–hydrogen chloride-catalysed homogeneous reaction, since butyl-lithium and butyl-lithium–hydrogen chloride do not act as catalysts in this reaction. (*c*) The rapid decrease in catalytic activity of these systems shows them to be very different from the homogeneous systems which we have previously studied. (*d*) The fact that cyclic dimer is produced directly, whereas in the case of the homogeneous reaction linear dimer is first formed, which is then converted into cyclic dimer,[1] also shows that this reaction is not of the normal homogeneous type. (*e*) Experiments designed to show exactly where the catalytic activity is situated (Results, Section 4) demonstrate conclusively that the activity resides in the precipitate and not in the supernatant liquid.

Reaction of Butyl-lithium with Titanium Tetrachloride.—Our results show that when titanium tetrachloride is added to butyl-lithium free tetrachloride is observed only when [LiBu]/[$TiCl_4$] <1, and that in the reverse order of addition free butyl-lithium is observed only when [LiBu]/[$TiCl_4$] >3. In order to explain these results we postulate the following reactions.

(*a*) When [LiBu]/[$TiCl_4$] >1 (excess of tetrachloride in supernatant liquid)

$$LiBu + TiCl_4 \longrightarrow TiCl_3 + LiCl + Bu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

It is likely that the precipitate formed by the reaction of butyl-lithium with tetrachloride consists of $TiCl_3$ and not $TiCl_3Bu$, since Bawn and Gladstone [9] have found that $TiCl_3Et$ is liquid at room temperature, and is readily soluble in hydrocarbons.

(*b*) When [LiBu]/[$TiCl_4$] > 3 (excess of alkyl in supernatant liquid)

$$3LiBu + TiCl_4 \longrightarrow \underset{\text{ppt.}}{TiCl_3(2LiBu)} + LiCl + Bu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where 2 butyl-lithium molecules form a complex with the trichloride. It is necessary to postulate that a complex is formed, and not lithium chloride, since the slow stepwise addition of small quantities of titanium tetrachloride to a butyl-lithium solution finally gives excess of tetrachloride only when [LiBu]/[$TiCl_4$] < 1 (see Results, Section 3a). This means that these two butyl-lithium molecules can be removed easily from this complex by the tetrachloride as follows:

$$\underset{\text{ppt.}}{TiCl_3(2LiBu)} + 2TiCl_4 \longrightarrow \underset{\text{ppt.}}{3TiCl_3} + 2LiCl + 2Bu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and this would not be possible if they had reacted with the titanium trichloride to form lithium chloride.

Friedlander and Oita [10] mixed butyl-lithium and titanium tetrachloride in benzene and found that free butyl-lithium was present in the supernatant liquid only when the [LiBu]/[$TiCl_4$] ratio was >3. For a [LiBu]/[$TiCl_4$] ratio of unity, they state that about 50% of the tetrachloride was reduced to the tervalent state, whereas at higher [LiBu]/[$TiCl_4$] ratios less reduction took place.

[9] Bawn and Gladstone, *Proc. Chem. Soc.*, 1959, 227.
[10] Friedlander and Oita, *Ind. Eng. Chem.*, 1957, **49**, 1885.

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Reaction Mechanism.—Our results show that the butyl-lithium–titanium tetrachloride system is not active for the dimerisation of 1,1-diphenylethylene unless hydrogen chloride is present. Even when butyl-lithium and titanium tetrachloride concentrations more equivalent to the monomer concentrations were used (Results, Section 5) still reaction was not observed. Thus the dimerisation of this olefin by the addition of the butyl group to the monomer molecule appears to be impossible in these circumstances. It is clear, therefore, that the activating group in the titanium tetrachloride–butyl-lithium–hydrogen chloride system is the proton from the hydrogen chloride.

Hydrogen chloride is in some way involved in the reaction which occurs on the surface of the precipitate. There is also hydrogen chloride in the supernatant liquid, since addition of titanium tetrachloride to this after filtration (Results, Section 4) brings about the homogeneous reaction catalysed by tetrachloride–hydrogen chloride. An equilibrium must exist therefore between the hydrogen chloride in the supernatant liquid and on the precipitate.

It is likely that the chlorine of the hydrogen chloride will be attracted to the titanium ions on the surface of the precipitate, to give a very active acid grouping. For a given concentration of hydrogen chloride the catalytic activity of the system is a maximum when 2 molecules of butyl-lithium are associated with the titanium trichloride. We consider this association to be such as not to involve replacement of the chlorine atoms by butyl groups, but to have sufficient interaction to cause a significant increase in the unsaturated nature of the titanium, and hence a marked increase in the catalytic activity of the complex. As the [LiBu]/[$TiCl_4$] ratio is increased above 3, the initial rate of reaction is reduced to zero. This loss of catalytic activity is, we believe, due to the removal of hydrogen chloride by the excess of alkyl in the irreversible reaction

$$LiBu + HCl \longrightarrow LiCl + BuH \quad . . . . . (4)$$

Proton transfer from the hydrogen chloride on the catalyst surface to a monomer would produce the $CH_3{\cdot}CPh_2^+$ ion, and give a resulting negative charge on the surface. This monomer ion, held to the surface by Coulombic attraction, could transfer a proton back to the surface, and so re-form the monomer molecule, or it could react with another monomer molecule to form a dimer ion which would also be held to the surface by Coulombic attraction. The return of a proton from the dimer ion to the surface would result in the formation of a dimer molecule. The fact that under these conditions only cyclic dimer is detectable in the reaction product, suggests that the surface tends to cause the two monomers to combine in this special way.

Order of Addition of Reagents.—If hydrogen chloride is added to the reaction mixture before the butyl-lithium (instead of afterwards, as is the normal case), we find that the initial rate is much slower. We believe this to be due to the fact that, when the alkyl is added to a system which already contains hydrogen chloride it reacts with it according to equation (4), and it is this reduction in the concentration of hydrogen chloride and butyl-lithium which slows down the reaction. When this alkyl is added to the titanium tetrachloride–olefin system before the hydrogen chloride, however, it is incorporated into the precipitate according to equation (2) and the system to which the hydrogen chloride is then added does not contain any free butyl-lithium by which it could be removed. The rapid fall in catalytic activity of the system in the initial stages (Fig. 5) may be due to reaction between the hydrogen chloride and the complexed butyl-lithium molecules in the precipitate. It is significant in this respect that the greatest initial fall in catalytic activity is for those systems ([LiBu]/[$TiCl_4$] ratio = 3) which have the greatest number of complexed butyl-lithium molecules, *i.e.*, 2.

Colour of Supernatant Liquid.—We found that for olefin–butyl-lithium–titanium tetrachloride–benzene systems in which the [LiBu]/[$TiCl_4$] ratio was between 1·19 and 2·0 the colourless supernatant liquid became yellow on addition of hydrogen chloride. To

examine this further, such a system was filtered by the high-vacuum technique [Experimental, Section 2 (b)], and the yellow filtrate divided into two parts. To one portion titanium tetrachloride was added. No precipitate was formed, showing the absence of free butyl-lithium in the supernatant liquid. This was also confirmed by the fact that the spectrum of the solution (Fig. 6) did not show the characteristic peak of the 1,1-diphenylhexyl anion.[8] Another portion of the filtrate was treated with butyl-lithium (more than enough to neutralise the hydrogen chloride present), and a dark brown precipitate

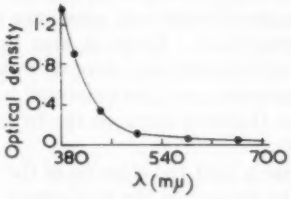

FIG. 6. *Spectrum of the supernatant liquid of a 1,1-diphenylethylene–butyl-lithium–titanium tetrachloride–hydrogen chloride–benzene system of* [LiBu]/[$TiCl_4$] *ratio* 1·3.

was formed immediately. This suggests the presence of some titanium tetrachloride in the supernatant liquid after the addition of hydrogen chloride. If this is the case, its amount, as estimated from the spectrum, is less than 10% of the total tetrachloride. For olefin–butyl-lithium–titanium tetrachloride–benzene systems in which the [LiBu]/[$TiCl_4$] ratio was between 2·0 and 3·0, the colourless supernatant liquid underwent no change on addition of hydrogen chloride; excess of butyl-lithium, therefore, prevents this action of hydrogen chloride on the precipitate.

Effect of Temperature.—Since the activity of the catalyst requires the association of hydrogen chloride with the precipitate, and the most active precipitate contains two butyl-lithium molecules complexed with titanium trichloride, it is not surprising that an increase in temperature reduces the catalytic activity of the system, and gives an apparent activation energy of −11·0 kcal. $mole^{-1}$.

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338. *Heterocyclic Polyfluoro-compounds. Part I. Pentafluoropyridine.**

By R. E. BANKS, A. E. GINSBERG, and R. N. HASZELDINE.

Pentafluoropyridine has been prepared by defluorination of undecafluoropiperidine. Infrared spectroscopy reveals a characteristic ring vibration near 1497 $cm.^{-1}$ for pentafluoropyridine and suggests that appreciable aromatic character is associated with the ring.

THE literature contains reference to the preparation of only monofluoropyridines,[1,2] except for a claim concerning an unidentified difluoropyridine.[2] Pentafluoropyridine has now

* Preliminary communication, *Proc. Chem. Soc.*, 1960, 211.

[1] Roe and Hawkins, *J. Amer. Chem. Soc.*, 1947, **69**, 2443; Simons, U.S.P. 2,447,717/1948; *J. Electrochem. Soc.*, 1949, **95**, 47; Hawkins and Roe, *J. Org. Chem.*, 1949, **14**, 328; Bradlow and Vanderwerf, *ibid.*, p. 509; Roe, Cheek, and Hawkins, *J. Amer. Chem. Soc.*, 1949, **71**, 4152; Minor, Hawkins, Vanderwerf, and Roe, *ibid.*, p. 1125; Beaty and Musgrave, *J.*, 1952, 875; Cava and Weinstein, *J. Org. Chem.*, 1958, **23**, 1616; Finger and Starr, *J. Amer. Chem. Soc.*, 1959, **81**, 2674.

[2] Simons and Herman, Abs. Amer. Chem. Soc. Meeting, Sept. 1947, p. 13J.

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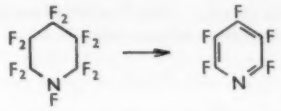
been prepared by defluorination of undecafluoropiperidine on a clean iron surface at 580—610°/<1 mm., with a particularly short contact time of ~1 sec.:



Undecafluoropiperidine is readily prepared, albeit in low yield, by the electrochemical fluorination of pyridine,[3] and hence a convenient two-stage conversion of pyridine into pentafluoropyridine can be effected.

The aromatisation of cyclic fluorocarbons by defluorination with hot nickel or, preferably, iron was first applied to the preparation of hexa- and penta-fluorobenzene from highly fluorinated cyclohexadienes.[4] The reaction was then extended to a range of alicyclic fluorocarbons and shown to provide a useful general route to aromatic fluorocarbons.[5] The defluorination of alicyclic fluorocarbons, however, requires the use of long contact times (10—30 min.) at atmospheric pressure. Thus, while octafluorotoluene is formed in 25% yield by defluorination of perfluoro(methylcyclohexane) at 500° at atmospheric pressure with a long contact time, we find that perfluoro(methylcyclohexane) is recovered unchanged after contact with iron at 700° for 1 sec. at 1 mm. pressure. Clearly, in the aromatisation of undecafluoropiperidine to pentafluoropyridine the N–F bond appreciably facilitates defluorination.

Pentafluoropyridine is a colourless, almost odourless, mobile liquid, b. p. 83·3°; as noted earlier,[6] replacement of a =CF– group by =N– in fluorocarbons has little effect on the boiling point (C_6F_6 has b. p. 81°). The aromatic character of pentafluoropyridine is revealed by the characteristic ring vibration at 1497 cm.$^{-1}$ in the infrared spectrum of its vapour, close to that (1536 cm.$^{-1}$) in hexafluorobenzene.[7]

Since the preliminary communication regarding this work, other workers [8] have reported the preparation of pentafluoropyridine in *ca.* 12% yield by defluorination of undecafluoropiperidine with nickel at 560° at atmospheric pressure.

Experimental

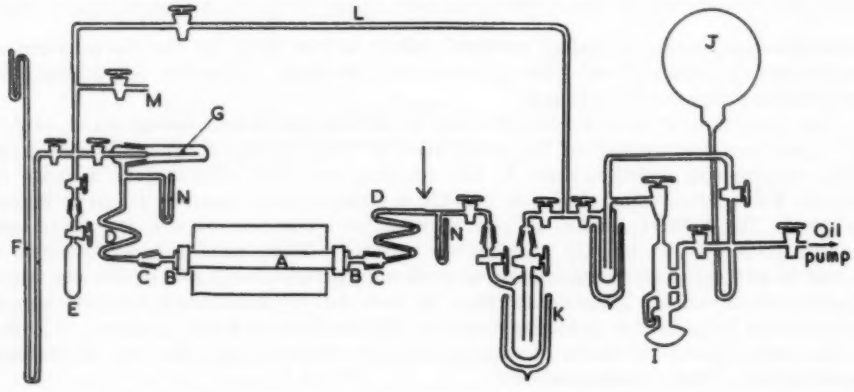
Preparation of Undecafluoropiperidine.—A 3·35 mole % solution of pyridine in anhydrous hydrogen fluoride was electrolysed at 25 amp. and 5·5 v (current density 0·0044 amp./cm.^{2}) in the electrochemical fluorination apparatus described previously.[9] After an induction period of *ca.* 400 amp. hr., during which free fluorine and/or oxygen difluoride was evolved from the cell, product began to collect at the rate of 8·96 g./Faraday in the trap cooled to −78°. Crude undecafluoropiperidine (yield, 8%), b. p. 46—55°, was separated from this product, which consisted mainly of perfluoropentane, by distillation through a 45 cm. × 1·2 cm. column packed with 2 mm. Fenske glass helices. Pure undecafluoropiperidine (Found: C, 21·1; N, 4·9%; *M*, 285. Calc. for $C_5F_{11}N$: C, 21·2; N, 4·95%; *M*, 283), b. p. 49°, was obtained from the crude material by means of large-scale gas chromatography (column, dinonyl phthalate–Celite; 75°; N_2 flow-rate, 10 l./hr.).

Preparation of Pentafluoropyridine.—The low-pressure defluorination apparatus is shown in Fig. 1. The pyrolysis section consisted of a nickel tube A (25″ long × 0·75″ i.d.) packed tightly with fine iron wire (100 g.) and heated electrically over 16″ of its length. The tube was connected to the " Pyrex " glass vacuum-system by means of adaptors (B) made from $\frac{7}{8}$″ o.d. mild-steel " Ermeto " couplings (Fig. 2). The seals made by these couplings remained leak-free

[3] Simons, U.S.P. 2,519,983/1950; Simmons *et al.*, *J. Amer. Chem. Soc.*, 1957, **79**, 3429.
[4] Banks, Barbour, Tipping, Gething, Patrick, and Tatlow, *Nature*, 1959, **183**, 586.
[5] Gething, Patrick, Stacey, and Tatlow, *Nature*, 1959, **183**, 588; Coe, Patrick, and Tatlow, *Tetrahedron*, 1960, **9**, 240.
[6] Haszeldine, *J.*, 1951, 102.
[7] Birchall and Haszeldine, *J.*, 1959, 13.
[8] Burdon, Gilman, Patrick, Stacey, and Tatlow, *Nature*, 1960, **188**, 231.
[9] Haszeldine and Nyman, *J.*, 1956, 2684.

even under a vacuum of 10^{-6} cm. Hg with the centre portion of the nickel tube at 800°. Heat conduction along the adaptors was almost eliminated by reducing the wall thickness of the stainless-steel tubing from $\frac{1}{8}$″ to $\frac{1}{56}$″ over a length of 1·5″. This enabled the final glass-to-metal joints (C) to be secured with picein. The flexible glass spirals (D) were necessary for the removal of the pyrolysis section from the vacuum line.

FIG. 1.



During a defluorination experiment, fluorocarbon contained in trap E under its own vapour pressure (measured by the manometer F) passed through the capillary G into the pyrolysis section, which was evacuated continuously by a mercury diffusion pump I backed by a 10 l. storage bulb J initially evacuated to 10^{-4} cm. Hg. E was immersed in a water-bath held at

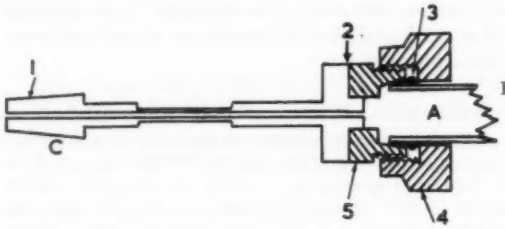


FIG. 2. 1, *Stainless steel*, B.14 *cone*; 2, *silver solder*; 3, "*Ermeto*" *ring*; 4, "*Ermeto*" *nut*; 5, *one half of an* "*Ermeto*" *coupling body*.

25° to enable the perfluoropiperidine to evaporate at an approximately constant rate. The pressure in the pyrolysis tube was measured by the manometers N. The defluorination product was condensed in trap K which was cooled to −196°; uncondensed gases collected in bulb J. The line L enabled the product in trap K to be returned, if necessary, to trap E for re-cycling. Before each defluorination experiment, the iron wire was activated at 650°/10 mm. Hg by dry hydrogen which was metered slowly into the apparatus at M.

In a typical preparation of pentafluoropyridine, undecafluoropiperidine (6·2 g.) was defluorinated at 600°/<1 mm. Hg (contact time <1·7 sec.) to give an almost colourless liquid product (2·3 g.) shown by analytical gas chromatography (column, dinonyl phthalate–Celite) to consist mainly of three components, none of which was undecafluoropiperidine. The component with the longest retention time (35 min., compared with 2 min. 9 sec. and 2 min. 52 sec.) was *pentafluoropyridine* (Found: C, 35·6; N, 8·3%; *M*, 165. C_5F_5N requires C, 35·5; N, 8·3%; *M*, 169), m. p. −41·5°, n_D^{20} 1·3856, separated in 26% yield from the defluorination product by large-scale gas–liquid chromatography. The other 74% of the defluorination product contained unsaturated heterocyclic fluorocarbons.

The vapour pressure of pentafluoropyridine, measured over the temperature range 0—90°, is given by the equation $\log_{10} p = 8{\cdot}20—1898/T$, where p is in mm. The calculated b. p. is 83·3°, Trouton's constant is 24·4, and the latent heat of vaporisation is 8685 cal. mole.$^{-1}$.

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Pentafluoropyridine was not formed when undecafluoropiperidine was defluorinated at 500°/221 mm. (contact time 4 min.), although the piperidine was completely converted into unsaturated heterocyclic fluorocarbons. For this experiment the capillary G was placed after the pyrolysis section at the position arrowed in Fig. 1, and the pressure in the pyrolysis tube was measured by manometer F. Defluorination of undecafluoropiperidine at 620°/<1 mm. gave pentafluoropyridine in *ca.* 20% yield, but at 700°/<1 mm. the organic material was almost completely destroyed and the iron became coated with a carbonaceous film.

One of the authors (A. E. G.) is indebted to the Carl Duisberg Stiftung (Leverküsen, Germany) for a maintenance grant. Support from Pennsalt Chemicals Corporation is gratefully acknowledged.

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339. *Rearrangement of Sulphonhydrazides.*

By P. CARTER and T. S. STEVENS.

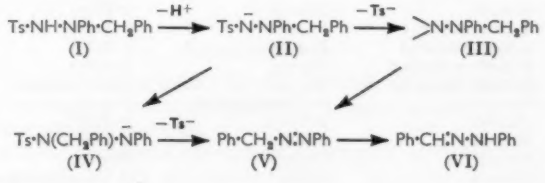
A series of sulphonhydrazides, R·CH$_2$·NR′·NH·SO$_2$R″, with alkali gave hydrazones, R·CH:N·NHR′, and sulphinic acid, H·SO$_2$R″. The change is intramolecular and shows first-order kinetics with respect to the anion of the hydrazide. The effect of substitution on the rate of reaction is discussed.

THE rearrangement of tertiary amines,[1]

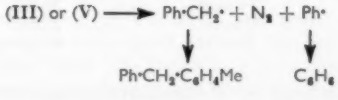
$$\text{Ph·CO·CH}_2\text{·NPh·CH}_2\text{Ph} \longrightarrow \text{Ph·CO·CH(CH}_2\text{Ph)·NHPh}$$

suggests the possibility of an analogous transformation in which the methylene group of the phenacyl radical is replaced by NH, *i.e.*, a rearrangement of *N*′-acyl-*N*-aryl-*N*-benzylhydrazines. Compounds of this type in which the acyl group was benzoyl were very resistant to alkali, but *N*-benzyl-*N*-phenyl-*N*′-toluene-*p*-sulphonylhydrazine afforded benzaldehyde phenylhydrazone with alkali toluenesulphinate: Ts·NH·NPh·CH$_2$Ph ⟶ Ph·NH·N:CHPh + TsH (Ts = *p*-C$_6$H$_4$Me·SO$_2$).

The reaction is rapid in hot dilute aqueous or alcoholic alkali, giving >60 moles % of benzaldehyde phenylhydrazone with ~30% of benzene. An oily by-product (~20% as C$_{14}$H$_{14}$), free from nitrogen and sulphur, resembles diphenylmethane and may be mixed phenyltolylmethanes from dimerisation of benzyl radicals. It seems admissible to write the alternative formulations



with the side-reactions:



The sequence (I) ⟶ (II) ⟶ (IV), analogous to the significant stages of the rearrangement of tertiary amines, seems an improbable mechanism, as it would be expected to be a slower process than the amine transformation (unless the tardiness of the latter is improbably attributed to difficulty in the initial extraction of a proton from the

[1] Cockburn, Johnstone, and Stevens, *J.*, 1960, 3340.

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phenacyl-methylene group), whereas the production of (VI) from (I) is very easy. The effect of substitution on the rate of reaction (see below) also tells against this view. The alternative scheme by way of (III) is taken as a provisional basis for discussion, with some reservations. While it is hard to avoid the assumption that the azo-compound (V) is an intermediate, there is no evidence for this; indeed, substituted *N*-benzyl-*N*-phenylhydrazines are oxidised by mercuric oxide to aldehyde arylhydrazones [2] under conditions unlikely to effect the isomerisation of the azo-compound (V), suggesting the possibility that the ion (II) yields the product (VI) otherwise than *via* (V). There is, further, no formal proof that it is the benzyl and not the phenyl group in (I) which migrates to the adjacent nitrogen atom, though this is no doubt more likely.

A similar reaction was shown by analogues of (I) substituted in either phenyl group or with sulphonyl radicals other than toluene-*p*-sulphonyl. *N*-Benzyl-*N*-2-naphthyl-*N'*-toluenesulphonylhydrazine gave benzaldehyde 2-naphthylhydrazone in moderate yield, with much naphthalene. *N*-Allyl-*N*-phenyl-*N'*-toluenesulphonylhydrazine * gave what appeared to be acraldehyde phenylhydrazone. On the other hand, the *N*-methyl and *N*-phenethyl analogues were hydrolysed without recognisable production of hydrazone, while *NN*-diphenyl-*N'*-toluenesulphonylhydrazine was unaffected by boiling dilute alkali. *NN*-Dibenzyl-*N'*-toluenesulphonylhydrazine gave, very easily, nitrogen and bibenzyl, as observed by Carpino.[3]

The process is substantially intramolecular. A mixture of *N*-benzyl-*N*-*p*-chlorophenyl-*N'*-toluenesulphonylhydrazine and *N*-*p*-chlorobenzyl-*N*-phenyl-*N'*-toluenesulphonylhydrazine (which react separately at a rather similar rate) gave with alkali a mixture of benzaldehyde *p*-chlorophenylhydrazone and *p*-chlorobenzaldehyde phenylhydrazone in which no benzaldehyde phenylhydrazone could be detected.

The kinetics of the reactions were examined, rather roughly, by titration with acid, the progressive replacement of the more basic anions (II) by toluenesulphinate being determined. On the scheme formulated, this involves following the process as far as (III) or (V), the stages (II) ⟶ (III) or (II) ⟶ (IV) being presumably rate-determining. The reaction is of the first order with respect to the anion of the hydrazide, and the velocity is unaffected by alkali in excess of one molecular proportion.

The effect of structural changes on the velocity of reaction is summarised in Table 1.

TABLE 1. *Alkaline decomposition of* $RR'N{\cdot}NH{\cdot}SO_2R''$.

No.	R	R′	R″	10^4k_1
1	Benzyl	Phenyl	*p*-Tolyl	3·3
2	4-Chlorobenzyl	Phenyl	*p*-Tolyl	1·9
3	4-Methylbenzyl	Phenyl	*p*-Tolyl	2·9
4	4-Methoxybenzyl	Phenyl	*p*-Tolyl	4·0
5	2-Methylbenzyl	Phenyl	*p*-Tolyl	3·4
6	Benzyl	*p*-Chlorophenyl	*p*-Tolyl	1·5
7	Benzyl	*p*-Tolyl	*p*-Tolyl	7·2
8	Benzyl	*o*-Tolyl	*p*-Tolyl	9·3
9	Benzyl	Phenyl	Phenyl	3·3
10	Benzyl	Phenyl	*p*-Nitrophenyl	3·6
11	Benzyl	Phenyl	*p*-Chlorophenyl	3·4
12	Benzyl	Phenyl	*o*-Tolyl	5·7
13	Benzyl	Phenyl	Methyl	1·2
14	Benzyl	Phenyl	Ethyl	1·6
15	Benzyl	Phenyl	Isopropyl	4·7

The reaction is somewhat hindered by electron-attracting substituents in the *N*-phenyl group, and to a less extent by such substituents in the benzyl radical. Electron-attracting substituents in the sulphonyl radical have a small accelerating effect; while such a

* Here and elsewhere the *para*-compound.

[2] Busch and Lang, *J. prakt. Chem.*, 1936, **144**, 291.
[3] Carpino, *J. Amer. Chem. Soc.*, 1957, **79**, 4427.

substituent will stabilise the sulphinate ion to be split off, it will to a similar extent reduce that basic character of $\bar{N}$ (formula II) which presumably supplies much of the driving force for the reaction; a quite small overall effect is thus not surprising. The effect of substitution in the benzyl radical is opposite to, and very much smaller than, that observed in the electrophilic rearrangement of benzylphenacylammonium salts.[4] The reaction path (I) ⟶ (II) ⟶ (III) ⟶ (V) is analogous to that assigned to the Hofmann rearrangement, $R{\cdot}CO{\cdot}NHBr \longrightarrow R{\cdot}CO{\cdot}\bar{N}Br \longrightarrow R{\cdot}CO{\cdot}N\!\!<\!\!\!

phenylhydrazone). With sodium hydroxide, the hydrochloride gave *N-diphenylmethyl-N-phenylhydrazine*, prisms from ethanol–water (Found: C, 82·9; H, 6·8; N, 10·3. $C_{19}H_{18}N_2$ requires C, 83·2; H, 6·6; N, 10·2%). The *acetyl derivative*, crystallised from ethanol, had m. p. 165—166° (Found: C, 79·7; H, 6·4; N, 8·9. $C_{21}H_{20}N_2O$ requires C, 79·8; H, 6·3; N, 8·9%).

Other hydrazines were prepared by reducing the appropriate nitrosamine (method B). These, if liquid, were used without purification; *N*-benzyl-*N*-nitroso-*p*-toluidine [11] had

TABLE 2. *NN-Disubstituted N'-benzylidenehydrazines.*[a]

Substituents	M. p.	Found (%) C	H	N	Formula	Required (%) C	H	N	Parent hydrazine Method	Properties
2-Methylbenzyl phenyl	92°[b]	83·9	6·9	9·3	$C_{21}H_{22}N_2$	84·0	6·7	9·3	A	M. p. 52—53°
4-Methylbenzyl phenyl	94[c]	83·8	7·2	9·6	,,	,,	,,	,,	A	B. p. 116°/0·01 mm.
4-Methoxybenzyl phenyl[d]	70—71	73·4	7·2	12·9	$C_{14}H_{16}N_2O$	73·7	7·0	12·3	A	
Diphenylmethyl phenyl	112[b]	86·1	6·2	8·0	$C_{26}H_{22}N_2$	86·2	6·1	7·7	A	M. p. 74°
4-Chlorobenzyl phenyl	100[c]	74·6	5·5	8·9	$C_{20}H_{17}ClN_2$	74·9	5·3	8·7		M. p. 40—42 [14, e]
Benzyl *p*-chlorophenyl	120[b,f]	74·9	5·4	—	,,	,,	,,	,,	B	B. p. 195—198°/15 mm.
Benzyl 2-naphthyl	175—176[f,g]	85·4	6·1	8·6	$C_{24}H_{20}N_2$	85·7	6·0	8·3	B	M. p. 76—78°[c]
α-Methylbenzyl phenyl[h]	160[b]	79·5	6·6	9·2	$C_{21}H_{20}N_2O$	79·7	6·3	8·9	B[i]	B. p. 175—180°/13 mm.

[a] All compounds in this Table were crystallised from ethanol and are colourless unless otherwise stated. [b] Prisms. [c] Needles. [d] All data refer to the simple disubstituted hydrazine. [e] Prepared by refluxing 4-chlorobenzyl bromide (1 mol.) with phenylhydrazine (2 mols.) in benzene for 8 hr. Pale yellow. [g] Plates. [h] All data for *N-benzoyl-N'-α-methylbenzylphenylhydrazine*. [i] Method A gave mainly styrene.

m. p. 52°, and *N*-benzyl-*N*-nitroso-2-naphthylamine, 110°. *N-Benzyl-N-nitroso-p-chloroaniline* crystallised from ethanol in pale yellow prisms, m. p. 58° (Found: C, 63·4; H, 4·9; N, 10·8. $C_{13}H_{11}ClN_2O$ requires C, 63·3; H, 4·5; N, 11·4%). *9,10-Dihydro-10-nitrosophenanthridine*,[12] yellow plates (from ethanol), m. p. 95—96°, gave a positive Liebermann reaction (Found: C, 73·8; H, 4·7; N, 13·4. $C_{13}H_{10}N_2O$ requires C, 74·3; H, 4·3; N, 13·3%). In general, the nitrosamine (1 mol.) in acetic acid (4 mols.) was added to a stirred suspension of zinc dust (excess) in water, the temperature being kept below 30° (the high-melting, sparingly soluble *N*-benzyl-*N*-nitroso-2-naphthylamine was reduced at 70°). After several hours' stirring, the base was extracted from the filtered solution by ether; some secondary amine was often produced as well. 9,10-Dihydro-10-nitrosophenanthridine gave mixtures containing much dihydrophenanthridine; it was not reduced by lithium aluminium hydride. Known *NN*-disubstituted hydrazines prepared in this way were: benzyl *o*-tolyl,[2,13] m. p. 36—38° (benzylidene derivative, m. p. 93°); benzyl *p*-tolyl,[13] m. p. 36° (benzylidene derivative, m. p. 138°). In other cases the hydrazine was characterised as benzylidene derivative (Table 2).

Preparation of Sulphonhydrazides.—Not unexpectedly, the Schotten–Baumann procedure was unsuitable, and reaction of the hydrazine with sulphonyl chloride in presence of a tertiary base was usually unsatisfactory. Unless otherwise stated, the hydrazines named in Tables 3 and 4 were prepared by refluxing the hydrazine (2 mols.) in benzene with the sulphonyl chloride (1 mol.) for 3—8 hr. The benzene solution then contained hydrazide; the precipitate was the water-soluble hydrazine hydrochloride, sometimes accompanied by further, water-insoluble hydrazide. The hydrazide was usually recrystallised from ethanol. In some cases, unless a lower temperature was used, the hydrazine $R{\cdot}CH_2{\cdot}NR'{\cdot}NH_2$ gave much of the hydrazone, $R{\cdot}CH_2{\cdot}NR'{\cdot}N{:}CHR$; it is significant that *N'*-benzenesulphonyl-*N*-benzyl-*N*-phenylhydrazine

[11] Kohler, *Annalen*, 1887, **241**, 360.
[12] Cf. Pictet and Ankersmit, *Annalen*, 1891, **266**, 151.
[13] Votoček and Allan, *Coll. Czech. Chem. Comm.*, 1936, **8**, 313.
[14] Cf. Hörlein, *Chem. Ber.*, 1954, **87**, 463.

TABLE 3. NN-*Disubstituted* N′-*toluene*-p-*sulphonylhydrazines.*

Substituents	Yield (%)	M. p.	Found (%) C	H	N	S	Formula	Required (%) C	H	N	S
Benzyl phenyl	55 [a]	142—143°	68·0	5·6	8·2	9·2	$C_{20}H_{20}N_2O_2S$	68·2	5·7	8·0	9·1
2-Methylbenzyl phenyl	60 [a]	129	68·8	6·2	7·7	—	$C_{21}H_{22}N_2O_2S$	68·9	6·0	7·7	8·7
4-Methylbenzyl phenyl	75 [a]	140	68·6	6·1	7·5	8·5		"	"	"	"
4-Methoxybenzyl phenyl	68 [b]	97—98	65·9	6·0	7·6	8·0	$C_{21}H_{22}N_2O_3S$	66·0	5·8	7·3	8·4
4-Chlorobenzyl phenyl	70 [a]	135—136	62·1	5·1	7·4	8·4 [c]	$C_{20}H_{19}ClN_2O_2S$	62·1	4·9	7·3	8·3
4-Nitrobenzyl phenyl [d]	20 [e]	161	60·3	4·9	10·8	7·8	$C_{20}H_{19}N_3O_4S$	60·5	4·8	10·6	8·0
Benzyl *o*-tolyl [a]	50 [b]	117	68·8	5·9	7·6	—	$C_{21}H_{22}N_2O_2S$	68·9	6·0	7·7	—
Benzyl *p*-tolyl	30 [b]	149	68·7	6·1	7·7	—		"	"	"	"
Benzyl *p*-chlorophenyl [f]	25 [b]	161	61·9	5·1	7·4	8·7	$C_{20}H_{19}ClN_2O_2S$	62·1	4·9	7·3	8·3
Benzyl 2-naphthyl	35 [b]	167	71·4	5·6	7·0	7·9	$C_{24}H_{22}N_2O_2S$	71·7	5·5	7·0	8·0
Allyl phenyl [g]	70 [a]	101	63·5	6·1	9·1	—	$C_{16}H_{18}N_2O_2S$	63·5	6·0	9·3	—
Methyl phenyl [h]	20 [i]	135—136	60·7	5·9	10·1	—	$C_{14}H_{16}N_2O_2S$	60·9	5·8	10·1	—
Phenethyl phenyl	48 [a]	105—106	68·6	6·1	7·7	8·4	$C_{21}H_{22}N_2O_2S$	68·9	6·0	7·7	8·7
Dibenzyl	80 [i]	125	68·9	6·0	7·7	8·9		"	"	"	"
Diphenyl		139—141 [j]	—	—	8·4	—	$C_{18}H_{16}N_2O_2S$	—	—	8·3	—

[a] Prisms. [b] Needles. [c] Found: Cl, 9·3. Req.: Cl, 9·2%. [d] Prepared in pyridine (95°; 3 hr.); yellow. [e] Prepared in boiling ether (48 hr.). [f] Reaction product separated by carbon tetrachloride into less-soluble hydrazide and more-soluble *N*-benzyl-*N*-toluenesulphonyl-*p*-chloroaniline (mixed m. p.). [g] Prepared in boiling ether (24 hr.). [h] Prepared in boiling ether (30 min.). [i] Plates. [j] Cubes.

TABLE 4. N-*Benzyl*-N-*phenyl*-N′-*sulphonylhydrazines.*

Acyl group	Yield (%)	M. p.	Found (%) C	H	N	Formula	Required (%) C	H	N
Benzenesulphonyl	50	119° [a]	67·2	5·4	8·3	$C_{19}H_{18}N_2O_2S$	67·5	5·3	8·3
Toluene-*o*-sulphonyl [b]	60	111 [c]	67·8	5·7	7·8	$C_{20}H_{20}N_2O_2S$	68·2	5·7	8·0
p-Chlorobenzenesulphonyl	60	157 [d]	60·8	4·6	7·4	$C_{19}H_{17}ClN_2O_2S$	61·2	4·6	7·5
p-Nitrobenzenesulphonyl [e]	70	178—179 [a]	59·5	4·6	11·3	$C_{19}H_{17}N_3O_4S$	59·5	4·4	11·0
Methanesulphonyl	35	119—120 [a]	60·8	5·7	9·7	$C_{14}H_{16}N_2O_2S$	60·8	5·8	10·0
Ethanesulphonyl	—	119—120 [a]	62·0	6·2	9·7	$C_{15}H_{18}N_2O_2S$	62·1	6·2	9·7
Propane-2-sulphonyl	45	100 [a]	63·0	6·7	9·4	$C_{16}H_{20}N_2O_2S$	63·2	6·6	9·2

[a] Needles. [b] Prepared in boiling ether (3 days). [c] Prisms. [d] Plates. [e] Yellow. [f] Found: S, 10·3. Req.: S, 10·5%.

decomposes at 120° with vigorous effervescence, giving benzaldehyde, recognised as 2,4-dinitrophenylhydrazone (18%). *p*-Chlorobenzene-,[15] *p*-nitrobenzene-,[16] methane-,[17] ethane-,[17] and propane-2-sulphonyl [17] chlorides were prepared by known methods.

Neither toluenesulphonyl chloride nor methanesulphonyl chloride gave a hydrazide with *N*-diphenylmethyl-*N*-phenylhydrazine. Reaction in benzene or in pyridine gave only *sym*-tetraphenylethane and unchanged hydrazine. *N*-α-Methylbenzyl-*N*-phenylhydrazine gave no hydrazide with toluenesulphonyl chloride; with *p*-nitrobenzenesulphonyl chloride it gave no hydrazide, a little acetophenone (identified as 2,4-dinitrophenylhydrazone), and some 6% of N-α-*methylbenzyl*-p-*nitrobenzenesulphonanilide*, pale yellow needles (from ethanol), m. p. 182—184° (Found: C, 62·4; H, 4·8; N, 7·4. $C_{20}H_{18}N_2O_4S$ requires C, 62·8; H, 4·7; N, 7·3%).

Decomposition of Sulphonhydrazides.—(i) *N*-Benzyl-*N*-phenyl-*N*′-toluene-*p*-sulphonylhydrazine (2 g.) and 5% aqueous sodium hydroxide (30 ml.) were heated at 100° for 1 hr. with occasional shaking. The solid crystallised from ethanol–water, giving benzaldehyde phenylhydrazone (mixed m. p.; 740 mg.). Chlorination of the aqueous filtrate at 0° gave toluenesulphonyl chloride (mixed m. p.).

(ii) The sulphonhydrazide (4 g.) was decomposed with aqueous alkali, and the crude hydrazone shaken with ligroin (b. p. 40—60°; 20 ml.). This extracted a yellow oil which after chromatography on alumina (elution by ligroin) gave 200 mg. of a colourless, nitrogen-free oil smelling like diphenylmethane. Nitration with concentrated sulphuric acid–fuming nitric acid gave a solid, m. p. 160—165° (from ethanol). With alcoholic sodium hydroxide this gave the blue colour characteristic of 2,4,2′,4′-tetranitrodiphenylmethane (m. p. 172°; mixed m. p. 140°).

[15] Chem. Fabr. Weiler-Ter Meer, G.P. 385,049.
[16] Bell, *J.*, 1928, 2770.
[17] Johnson and Sprague, *J. Amer. Chem. Soc.*, 1936, **58**, 1348.

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(iii) The sulphonhydrazide (4 g.) was refluxed with 2% aqueous sodium hydroxide (150 ml.) for 1 hr., and 60 ml. were distilled. The distillate was shaken with ligroin (b. p. 60—80°) (30 ml.), and the extract distilled. Nitration of the fraction boiling below 80° gave *m*-dinitrobenzene (600 mg.; mixed m. p.); the higher-boiling portion gave benzaldehyde 2,4-dinitrophenylhydrazone (60 mg.; mixed m. p.).

Benzaldehyde phenylhydrazone was also produced in quantity by heating the sulphonhydrazide with solid potassium hydroxide at 140°, or by refluxing it for 2 hr. with sodium hydroxide in ethanol–water (2 : 1).

The other sulphonhydrazides were treated as in (i) above (aqueous ethanol was used as solvent in case 6 of Table 1), and the hydrazones had the properties described in the literature. In cases 2—5 and 7, identity was confirmed by mixed m. p. with authentic material.

N-*p*-Nitrobenzyl-*N*-phenyl-*N'*-toluenesulphonylhydrazine, with an excess of hot aqueous-ethanolic sodium hydroxide, gave a dark brown powder, m. p. >250°, insoluble in ethanol. Heated with 1 equiv. of alkli, the hydrazide yielded a red, uncrystallisable gum which gave a green colour with ethanolic alkali. With ethanolic sodium hydroxide, *p*-nitrobenzaldehyde phenylhydrazone gave a similar green colour and, on refluxing, an insoluble solid resembling that obtained from the hydrazide.

N-Benzyl-*N*-2-naphthyl-*N'*-toluenesulphonylhydrazine (3 g.) was refluxed for 2 hr. in ethanol with 10% aqueous sodium hydroxide (10 ml.). Ethanol was distilled off, water added, and the solid produced separated by ligroin into soluble naphthalene (420 mg.; mixed m. p.) and insoluble benzaldehyde 2-naphthylhydrazone (650 mg.; m. p. 194°).

N-Allyl-*N*-phenyl-*N'*-toluenesulphonylhydrazine (2 g.) gave with warm aqueous sodium hydroxide a steam-volatile oil which crystallised from ligroin as yellow plates (550 mg.), m. p. 47—48°. The compound, which is insoluble in dilute acid, does not give the violet colour with chromic acid characteristic of pyrazolines,[8] and immediately liquefies when mixed with 1-phenylpyrazoline (m. p. 52°), is regarded as *acraldehyde phenylhydrazone* (Found: C, 73·8; H, 7·0; N, 18·8. $C_9H_{10}N_2$ requires C, 73·9; H, 6·9; N, 19·2%). The infrared spectrum shows high maxima at 999 and 907 cm.$^{-1}$, consistent with the presence of a vinyl group.

N-Methyl-*N*-phenyl-*N'*-toluenesulphonylhydrazine (1 g.), with hot aqueous alkali, gave a steam-volatile, basic oil (200 mg.) which with benzaldehyde yielded benzaldehyde methylphenylhydrazone.

N-Phenethyl-*N*-phenyl-*N'*-toluenesulphonylhydrazine (1 g.), refluxed with 20% aqueous sodium hydroxide (50 ml.) for 4 hr., gave an oil, the basic portion of which yielded with benzaldehyde, benzaldehyde *N*-phenethyl-*N*-phenylhydrazone [10] (200 mg.; mixed m. p.).

Intramolecular Mechanism.—Equal amounts of *N*-benzyl-*N*-*p*-chlorophenyl-*N'*-toluenesulphonylhydrazine and *N*-4-chlorobenzyl-*N*-phenyl-*N'*-toluenesulphonylhydrazine were refluxed together with sodium hydroxide solution and the product (A) examined chromatographically, by capillary ascent on Whatman No. 1 paper, ethanol–water (1 : 2 by vol.) being used as solvent. The behaviour of product A was indistinguishable from that of a mixture of benzaldehyde *p*-chlorophenylhydrazone and *p*-chlorobenzaldehyde phenylhydrazone, and addition of 2% of benzaldehyde phenylhydrazone was easily detected. Spots were recognised by their fluorescence under ultraviolet light. Benzaldehyde phenylhydrazone had the R_F value 0·45, and each chlorinated hydrazone, 0·30.

Kinetics of the Reaction.—*N*-Benzyl-*N*-phenyl-*N'*-toluene-*p*-sulphonylhydrazine (1·00 g.) in ethanol (50 ml.) was mixed with 0·5N-aqueous sodium hydroxide (10 ml.: 1·77 equiv.) at 74·5° ± 0·1°. Successive portions (5 ml.) were withdrawn, added to cold water (20 ml.), and titrated with hydrochloric acid against phenolphthalein. Results of a typical run are given below; x = diminution in titre (equiv.) after time t(sec.).

t	600	1200	1800	2400	3000	3600	4800	6000	
x	0·20	0·34	0·45	0·52	0·63	0·69	0·76	0·86	
10^4k_1	3·7	3·5	3·3	3·1	3·3	3·3	2·9	3·3	Mean 3·3

An experiment in which one equiv. of alkali was used gave indistinguishable results. The results recorded in Table 1 were obtained in the same way.

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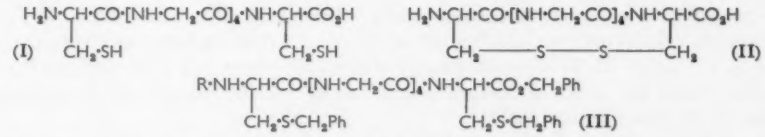
340. *Polypeptides. Part VI.*[1] *A Further Study of the Oxidation of* L-*Cysteinyl-tetraglycyl-*L-*cysteine.*

By D. G. Large, H. N. Rydon, and J. A. Schofield.

The oxidation of L-cysteinyl-tetraglycyl-L-cysteine (I) in dilute aqueous solution at pH 8·6 has been re-examined and the earlier conclusion [2] that this yields mainly the cyclic monomer, *SS'*-dehydro-L-cysteinyl-tetraglycyl-L-cysteine (II), has been confirmed.

In an earlier paper [2] it was concluded that the principal oxidation product produced by aeration of a dilute aqueous solution of L-cysteinyl-tetraglycyl-L-cysteine (I) at pH 8·6 was the cyclic, monomeric disulphide, *SS'*-dehydro-L-cysteinyl-tetraglycyl-L-cysteine (II). The evidence for this conclusion was somewhat indirect and the main object of the present work was to obtain support for it.



The fully protected hexapeptide (III; R = Ph·CH_2·O·CO·) was prepared in considerable quantity. Although the synthetic route was the same as that followed by Hooper *et al.*,[3] the process was considerably improved, giving a much higher overall yield than was obtained by these, and other,[4] workers. The main improvements were the preparation of the intermediates, *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-glycyl-glycine ethyl ester and *N*-benzyloxycarbonyldiglycyl-*S*-benzyl-L-cysteine benzyl ester, by coupling the appropriate cysteine and glycyl-glycine derivatives by means of bis-*o*-phenylene pyrophosphite [5] and a greatly improved yield in the final coupling of *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-glycyl-glycine azide with diglycyl-*S*-benzyl-L-cysteine benzyl ester.

In our first experiments, the fully protected hexapeptide (III; R = Ph·CH_2·O·CO·), or the hydrobromide of the partially protected peptide (III; R = H) obtained from it by the action of hydrogen bromide in acetic acid,[6] was treated with sodium in liquid ammonia, and the resulting free hexapeptide (I) was oxidised, without isolation, by passing air or oxygen through its 1% aqueous solution at pH 8·6 until the nitroprusside reaction was negative. Paper electrophoresis in N-acetic acid, in the simple apparatus of Durrum,[7] showed the presence of one major, ninhydrin-positive, postively charged component, which was usually accompanied by up to four other similar substances, three moving more slowly (relative migration rates 0·45, 0·6, and 0·85) and one more quickly (relative rate 1·1) than the main product. Dinitrophenylation [8] of the crude oxidation mixture gave, as the main product, a 2,4-dinitrophenyl derivative chromatographically indistinguishable from that prepared earlier.[2] Attempts to isolate the main oxidation product in a state of purity by continuous paper electrophoresis [9] were frustrated, despite the good separation achieved, by poor recoveries of material. More success was achieved by counter-current distribution and a small amount of purified material was obtained by 150 transfers between s-butyl alcohol and 0·5% aqueous trichloroacetic acid. Material so purified still appeared,

[1] Part V, Benoiton and Rydon, *J.*, 1960, 3328.
[2] Heaton, Rydon, and Schofield, *J.*, 1956, 3157.
[3] Hooper, Rydon, Schofield, and Heaton, *J.*, 1956, 3148.
[4] Lautsch and Kraege, *Chem. Ber.*, 1956, **89**, 737.
[5] Crofts, Markes, and Rydon, *J.*, 1959, 3610.
[6] Ben-Ishai and Berger, *J. Org. Chem.*, 1952, **17**, 1564.
[7] Durrum, *J. Amer. Chem. Soc.*, 1950, **72**, 2943.
[8] Sanger, *Biochem. J.*, 1945, **39**, 507; Levy and Chung, *J. Amer. Chem. Soc.*, 1955, **77**, 2899.
[9] Durrum, *J. Amer. Chem. Soc.*, 1951, **73**, 4875.

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on paper electrophoresis, to contain traces of two other components (relative migration rates 1·10 and 1·27); these were not removed by a further 100 counter-current transfers and probably arise by a little disulphide interchange during the counter-current distribution or the electrophoresis.

Although the amount of purified material obtained in this way was very small, it was sufficient to enable the correctness of the monomeric cyclic structure (II) to be established in two independent ways. In the first method, the purified oxidation product was treated with a deficiency of 1-fluoro-2,4-dinitrobenzene in aqueous-ethanolic sodium hydrogen carbonate,[8] and the reaction mixture was examined by paper chromatography; apart from unchanged starting material and 2,4-dinitrophenol, only one, yellow, product was detected and it was chromatographically identical with the already mentioned 2,4-dinitrophenyl derivative; no ninhydrin-positive, yellow product, such as would undoubtedly have been produced had the oxidation product contained more than one amino-group,[10] could be detected, and it may safely be concluded that the major oxidation product is the monomeric disulphide (II). This conclusion was supported by cryoscopic determinations of the molecular weight of the oxidation product (Found: M, 381 $\pm$ 29. Calc.: M, 450) isopiestically in trifluoroacetic acid [11] and of the *N*-2,4-dinitrophenyl derivative (Found: M, 534 $\pm$ 7. Calc.: M, 617) cryoscopically in phenol. Our work thus confirms the earlier conclusion [2] that the major oxidation product of L-cysteinyl-tetraglycyl-L-cysteine (I) is the monomeric cyclic disulphide (II).

We made numerous attempts to devise a procedure for the preparation of the cyclic disulphide (II) pure and in quantity; although these failed, a number of incidental observations were made which seem worth recording. As with cysteine [12] and cysteinyl-cysteine,[13] the rate of oxidation of L-cysteinyl-tetraglycyl-L-cysteine (I) is markedly affected by pH, being complete at pH 8·6 in 30 minutes but incomplete even after 12 days at pH 4; oxidations at the latter, and lower, pH had, perforce, to be carried out with hydrogen peroxide. The effect of pH on the nature of the oxidation products of (I) is less marked than with cysteinyl-cysteine,[13] although in very strongly acid solution (pH 2) the cyclic monomer (II) was accompanied by another product, present in approximately equal amount, which moved much more slowly on electrophoresis but was not identified. As with cysteine,[14] oxidation of the dithiol (I) is strongly catalysed by metal ions: addition of ferric ions to the oxidation solution considerably reduced the amount of monomeric oxidation product (II) and increased the amount of by-products; conversely, addition of ethylenediaminetetra-acetic acid almost completely repressed the formation of by-products, the monomeric disulphide (II) becoming practically the sole oxidation product, not only at pH 8·6, but also at pH 10 and at pH 4 (oxidation with hydrogen peroxide). It seems that there may be two oxidation processes in operation side-by-side, one metal-catalysed and the other not, the former giving rise to a more complex range of oxidation products than the latter.

Experimental

Synthesis of S-*Benzyl*-N-*benzyloxycarbonyl*-L-*cysteinyl-tetraglycyl*-S-*benzyl*-L-*cysteine Benzyl Ester.*—*S*-Benzyl-L-cysteine [15] had m. p. 214—215°, $[\alpha]_D^{22.5}$ + 29·5° (*c* 1·0 in N-NaOH); care is necessary, when recrystallising the derived benzyl ester toluene-*p*-sulphonate from water, to avoid hydrolysis and consequential lowering of the optical rotation. *S*-Benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-glycyl-glycine ethyl ester, prepared in 59—65% yield by the method of

[10] Jarvis, Rydon, and Schofield, following paper.
[11] Schwyzer, Iselin, Rittel, and Sieber, *Helv. Chim. Acta*, 1956, **39**, 872.
[12] Mathews and Walker, *J. Biol. Chem.*, 1909, **6**, 21; Dixon and Tunnicliffe, *Proc. Roy. Soc.*, **1923**, *B*, **94**, 266; Benesch and Benesch, *J. Amer. Chem. Soc.*, 1955, **77**, 5877.
[13] Izumiya and Greenstein, *Arch. Biochem. Biophys.*, 1954, **52**, 203; Wade, Winitz, and Greenstein, *J. Amer. Chem. Soc.*, 1956, **78**, 373.
[14] Baumann, *Z. physiol. Chem.*, 1883, **8**, 299; Andreasch, *Monatsh.*, 1885, **6**, 821; Mathews and Walker, *J. Biol. Chem.*, 1909, **6**, 299; Schubert, *J. Amer. Chem. Soc.*, 1932, **54**, 4077.
[15] Wood and du Vigneaud, *J. Biol. Chem.*, 1939, **130**, 109.

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Crofts *et al.*,[5] had m. p. 111—112°, $[\alpha]_D^{20}$ −12·2° (*c* 2·2 in EtOH), and was converted into the hydrazide, m. p. 164·5—166°, in 75—87% yield by the method of Hooper *et al.*[3] *N*-Benzyloxycarbonyldiglycyl-*S*-benzyl-L-cysteine benzyl ester, prepared in 75—79% yield by the method of Crofts *et al.*,[5] had m. p. 114—115° or 122—124° (dimorphous), $[\alpha]_D^{22·5}$ −34·6° (*c* 0·5 in EtOH), and was converted into diglycyl-*S*-benzyl-L-cysteine benzyl ester hydrobromide, m. p. 147—149°, in 57—66% yield by treatment with hydrogen bromide in acetic acid.[3,10]

An ethyl acetate solution of the free peptide, obtained by dissolving the last mentioned hydrobromide (17·0 g.) in water (50 ml.) containing triethylamine (5 ml.) and extraction with ethyl acetate (200 ml. and 3 × 100 ml.), was dried over sodium sulphate and cooled to 0°. *S*-Benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-glycyl-glycine hydrazide (16·4 g.), in water (10 ml.), acetic acid (140 ml.), and concentrated hydrochloric acid (27·5 ml.), was cooled to 0° and treated with 20% aqueous sodium nitrite solution (17 ml.); the precipitated azide was extracted into cold ethyl acetate (4 × 200 ml.) and the extract washed, at 0°, with saturated sodium hydrogen carbonate solution (2·5 l.) and then dried (Na_2SO_4). The two filtered ethyl acetate solutions were mixed at 0° and the mixture was kept overnight at 0°. Next day, the precipitated peptide (27·7 g., 94%), m. p. 190—193°, was collected and washed with a little ethyl acetate. Recrystallisation from aqueous dimethylformamide and then from 90% ethanol gave the protected hexapeptide (20·0 g., 68%), m. p. 206—207°, $[\alpha]_D^{23}$ −34·5° (*c* 1·1 in pyridine) (lit.,[3] m. p. 205—206°, $[\alpha]_D^{20}$ −29·7°). In other experiments the yields varied between 51% and 75%.

This protected peptide (5·0 g.) was dissolved in acetic acid (50 ml.) containing hydrogen bromide (8·1 g.), and the mixture kept at 25° for 35 min., then poured into anhydrous ether (300 ml.) at 0°. The precipitated *S*-benzyl-L-cysteinyl-tetraglycyl-*S*-benzyl-L-cysteine benzyl ester hydrobromide (4·5 g., 95%) was collected by centrifugation and washed repeatedly with dry ether (2 l. in all).

Oxidation of L-*Cysteinyl-tetraglycyl-*L-*cysteine*.—Two procedures were used. In method A the sodium was removed, after the reduction, by means of an ion-exchange resin, the final product being substantially free from sodium salts; in method B, resin was not used and the final product was a mixture of the oxidation product and sodium bromide. The details of the two procedures were as follows (all operations involving the free dicysteine peptide were carried out in an inert atmosphere):

Method A. *S*-Benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-tetraglycyl-*S*-benzyl-L-cysteine benzyl ester, or *S*-benzyl-L-cysteinyl-tetraglycyl-L-cysteine benzyl ester hydrobromide, was dissolved in redistilled liquid ammonia (*ca.* 50 ml./g.), and sodium added (either in small pieces or as a solution in liquid ammonia), with stirring, until a permanent blue colour was obtained. Amberlite I.R.-120 resin (NH_4^+) was added in excess and the ammonia removed from the product by evaporation, finally under reduced pressure. The residue was treated with boiled-out distilled water, and the resin was filtered off and washed with a little water. After adjustment of the pH to the desired value (with aqueous hydrobromic acid, acetic acid, or carbon dioxide) the solution was diluted with water to bring the concentration of L-cysteinyl-tetraglycyl-L-cysteine to 1%. Oxygen or air was then passed through the solution until the nitroprusside reaction was negative. The pH of the solution was then adjusted to 5·5 and the solution concentrated to small volume under reduced pressure (bath-temp. 30—40°). The residue was treated with an excess of ethanol, and the precipitated solid collected by centrifugation, washed thrice with ethanol and twice with ether, and dried in a vacuum-desiccator.

Method B. The partially protected hexapeptide hydrobromide was reduced, by a weighed amount of sodium, as in Method A. When a permanent blue colour was obtained, ammonium bromide equivalent to the sodium used, less two g.-atoms per mole of peptide, was added. The solution was then evaporated and the residue dissolved in water, and oxidised and worked up as in Method A, two equivalents of hydrogen bromide per mole of peptide being added in the last stage.

Purification of the Oxidation Product by Counter-current Distribution.—The apparatus was a semi-automatic 50 tube, 25 ml. phase, apparatus (Quickfit and Quartz Ltd.). The solvent system was s-butyl alcohol–0·5% aqueous trichloroacetic acid, equilibrated by mechanical shaking overnight.

The oxidation was carried out, at pH 8·6, by method A. The oxidation product (1·76 g.; containing about 50% of ammonium carbonate) was dissolved in sufficient of the lower phase to bring the volume to 25 ml. and the solution placed in the first tube of the apparatus, lower phase (25 ml.) being placed in the other 49 tubes. Upper phase (25 ml.) was placed in the

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first four upper tubes and the distribution process carried out, with a shaking time of 2 min. and a settling time of 2½ min. Additional upper (moving) phase (25 ml.) was added to the first tube after each transfer.

Disulphide-containing material (positive cyanide–nitroprusside reaction) reached tube 50 after 152 transfers. Examination by paper-electrophoresis in N-acetic acid showed that the main product was present in tubes 42—50 (accompanied by very small amounts of material with relative electrophoretic migration rates of 1·30 and 1·10) and in tubes 36—41 (as tubes 42—50, with faint traces of materials with relative electrophoretic migration rates of 0·60 and 0·22).

The contents of the two sets of tubes were evaporated to dryness under reduced pressure; treatment of the residues with ethanol and ether gave the purified oxidation product (142 mg. from tubes 42—50; 308 mg. from tubes 36—41). A further distribution of the material from tubes 42—50 between the same pair of solvents (100 transfers) gave a product (35 mg.) still containing traces of the two faster-moving impurities (relative electrophoretic migration rates, 1·25 and 1·10).

Four determinations of the molecular weight of the twice purified product were carried out by the isopiestic method of Schwyzer *et al.*,[11] with 0·5—1·0% solutions in trifluoroacetic acid and L-cystine as reference substance. The values obtained in successive runs were 457, 349, 390, and 326; mean ± S.E., 381 ± 29.

Dinitrophenylation of the Oxidation Product.—The purified oxidation product (90 mg.), in water (7 ml.), containing sodium hydrogen carbonate (100 mg.), was stirred vigorously at room temperature for 3 hr. with 1-fluoro-2,4-dinitrobenzene (0·025 ml.). After acidification, the crude *N*-2,4-dinitrophenyl derivative (61·7 mg., 50%) was collected, washed with a little water, and dried. This derivative was applied, as a band, to Whatman 3 MM filter paper and the chromatogram developed with n-butyl alcohol–pyridine–water (39 : 21 : 39). Apart from some dinitrophenol, the only yellow material had R_F 0·57 and was ninhydrin-negative; this was eluted (from several papers) with 80% acetone and the combined eluates were evaporated under reduced pressure, affording the purified derivative (40 mg.).

Two determinations of the molecular weight of this derivative were carried out cryoscopically in phenol, with *N*-2,4-dinitrophenylglycine as reference substance; the values obtained were 542 and 527.

We thank the Department of Scientific and Industrial Research for a Research Studentship (D. G. L.) and Messrs. Imperial Chemical Industries Ltd. for the loan of apparatus.

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MANCHESTER, 1. [*Received, November 1st*, 1960.]

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341. *Polypeptides. Part VII.*[1] *The Synthesis and Oxidation of* L-*Cysteinyl-pentaglycyl*-L-*cysteine and* L-*Cysteinyl-hexaglycyl*-L-*cysteine.*

By D. JARVIS, H. N. RYDON, and (in part) J. A. SCHOFIELD.

N-Benzyloxycarbonyl-*S*-benzyl-L-cysteinyl-pentaglycyl-*S*-benzyl-L-cysteine benzyl ester (I; $n = 5$) and the corresponding hexaglycyl compound (I; $n = 6$) have been synthesised. Oxidation of L-cysteinyl-pentaglycyl- and -hexaglycyl-L-cysteine (II; $n = 5$ and 6), obtained by removal of the protecting groups, in dilute aqueous solution at pH 8·6, has been shown to produce almost exclusively the cyclic disulphides, *SS'*-dehydro-L-cysteinyl-pentaglycyl- and -hexaglycyl-L-cysteine (III; $n = 5$ and 6).

EARLIER papers in this series described the preparation[2] of a number of protected L-cysteinyl-polyglycyl-L-cysteines (I; $n = 0$—4) and the oxidation,[1,3] in dilute aqueous solution, of the derived free peptides (II; $n = 0$—4). It was found that the proportion

[1] Part VI, Large, Rydon, and Schofield, preceding paper.
[2] Hooper, Rydon, Schofield, and Heaton, *J.*, 1956, 3148.
[3] Heaton, Rydon, and Schofield, *J.*, 1956, 3157.

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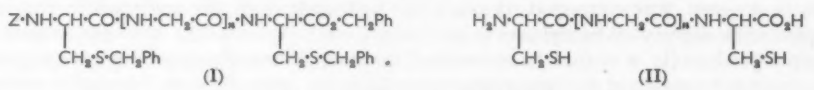
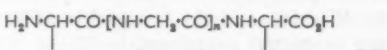
of monomeric cyclic disulphide (III) present in the oxidation products increased with increasing separation of the cysteine residues, the cyclic monomer becoming the major product in the case of the tetraglycyl compound (II; $n = 4$). At about the same time, Lautsch and Kraege [4] reported the oxidation of the hexapeptide (II; $n = 4$) to the monomeric cyclic disulphide (III; $n = 4$), but did not adduce any evidence for the structure assigned to their oxidation product.

Since the twenty-membered disulphide ring system present in (III; $n = 4$) is also found in Nature, in the hormones insulin,[5] oxytocin,[6] and the vasopressins,[7] it seemed important to study higher members of the series (II) in order to ascertain whether there was some critical factor tending to make the formation of such twenty-membered ring compounds particularly easy. While our work was in progress, Lautsch and his colleagues [8,9,10] reported, without experimental detail, the oxidation of L-cysteinyl-penta-, -hexa-, and -hepta-glycyl-L-cysteine (II; $n = 5$, 6, and 7) to the monomeric cyclic disulphides (III; $n = 5$, 6, and 7); only in the case of the octapeptide (III; $n = 6$) was the structure claimed for the oxidation product supported by experimental evidence (molecular weight). The same school has also announced [9,10,11] similar findings with other peptides in which two cysteine residues are separated by 4—6 other amino-acid residues.



(I) (II)



(III)

Here and elsewhere Z = Ph·CH$_2$·O·CO·

The key intermediates for the synthesis of the protected heptapeptide (I; $n = 5$) were *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-diglycyl-glycine ethyl ester (IV; $n = 3$) and *N*-benzyloxycarbonyldiglycyl-*S*-benzyl-L-cysteine benzyl ester (V; $n = 2$, R = Z). Both intermediates had previously been prepared by Hooper *et al.*,[2] but in both cases improved results were obtained by using di-*o*-phenylene pyrophosphite as coupling reagent.[12] The use of this reagent in the coupling of *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteine with diglycyl-glycine ethyl ester gave the first-named intermediate (IV; $n = 3$) with a much higher rotation than was obtained by the earlier workers [2] who had used the mixed anhydride method of coupling; [13] although racemisation does not generally occur in coupling reactions involving mixed anhydrides derived from *N*-benzyloxycarbonyl amino-acids,[14,15] the lability of derivatives of *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteine has been encountered by several workers [16] and it is not altogether surprising that couplings using

[4] Lautsch and Kraege, *Chem. Ber.*, 1956, **89**, 737.
[5] Ryle, Sanger, Smith, and Kitai, *Biochem. J.*, 1955, **60**, 541.
[6] du Vigneaud, Ressler, and Trippett, *J. Biol. Chem.*, 1953, **205**, 949; du Vigneaud, Ressler, Swan, Roberts, and Katsoyannis, *J. Amer. Chem. Soc.*, 1954, **76**, 3115; Tuppy, *Biochim. Biophys. Acta*, 1953, **11**, 449; Tuppy and Michl, *Monatsh.*, 1953, **84**, 1011.
[7] du Vigneaud, Lawler, and Popenoe, *J. Amer. Chem. Soc.*, 1953, **75**, 4880; du Vigneaud, Gish, and Katsoyannis, *ibid.*, 1954, **76**, 4751; Acher and Chauvet, *Biochim. Biophys. Acta*, 1953, **12**, 487.
[8] Lautsch, Wiechert, Gnichtel, Schuchardt, Kraege, Singewald, Broser, Becker, Rauhut, and Grimm, *Österr. Chem.-Ztg.*, 1957, **58**, 33.
[9] Lautsch, Wiemer, Zschenderlein, Kraege, Bandel, Günther, Schulz, and Gnichtel, *Kolloid Z.*, 1958, **161**, 36.
[10] Lautsch, Boroschewski, Gante, Shingte, Rauhut, Grimm, Rimpler, Schulz, and Paetzke, *Chimia* (*Switz.*), 1959, **13**, 142.
[11] Lautsch and Günther, *Naturwiss.*, 1957, **44**, 492; Lautsch and Schulz, *ibid.*, 1958, **45**, 58.
[12] Crofts, Markes, and Rydon, *J.*, 1959, 3610.
[13] Boissonnas, *Helv. Chim. Acta*, 1951, **34**, 874.
[14] Goodman and Kenner, *Adv. Protein Chem.*, 1957, **12**, 465.
[15] Vaughan, *J. Amer. Chem. Soc.*, 1952, **74**, 6137.
[16] For refs. see Young, *Coll. Czech. Chem. Comm.*, 1959, **24**, Special Issue, 114.

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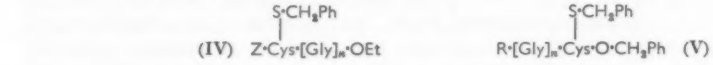
the derived mixed anhydride may be accompanied by racemisation. The second intermediate (V; $n = 2$, R = Z) was prepared in good yield by coupling *N*-benzyloxycarbonylglycyl-glycine and *S*-benzyl-L-cysteine benzyl ester with the aid of di-*o*-phenylene pyrophosphite;[12] this method gave a much better yield than the mixed anhydride procedure.[13] The *N*-benzyloxycarbonyl group was selectively removed from the protected peptide (V; $n = 2$; R = Z) with hydrogen bromide in acetic acid,[17] and the product (V; $n = 2$; R = H) treated with the azide obtained, through the hydrazide, from the protected tetrapeptide ester (IV; $n = 3$); the required protected heptapeptide (I; $n = 5$), so obtained, had properties in satisfactory agreement with those recorded by Lautsch and Kraege [4] for material synthesised by a different route.



(IV) Z·Cys(S·CH$_2$Ph)·[Gly]$_n$·OEt R·[Gly]$_n$·Cys(S·CH$_2$Ph)·O·CH$_2$Ph (V)

Two methods were used for the synthesis of the protected octapeptide (I; $n = 6$). In the first, the azide derived from *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-glycyl-glycine ethyl ester (IV; $n = 2$) [1,12] was coupled with glycyl-glycine ethyl ester to give *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-triglycyl-glycine ethyl ester (IV; $n = 4$). This, in its turn, was converted, through the hydrazide, into the azide which was then coupled with diglycyl-*S*-benzyl-L-cysteine benzyl ester (V; $n = 2$; R = H) to give the required product (I; $n = 6$). In the second method, *N*-benzyloxycarbonylglycyl-glycine was coupled, by means of di-*o*-phenylene pyrophosphite, with diglycyl-*S*-benzyl-L-cysteine benzyl ester (V; $n = 2$; R = H), and the benzyloxycarbonyl group was selectively removed from the resulting protected pentapeptide (V; $n = 4$; R = Z) with hydrogen bromide in acetic acid.[17] Tetraglycyl-*S*-benzyl-L-cysteine benzyl ester (V; $n = 4$; R = H), so obtained, was treated with the azide from *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-glycyl-glycine ethyl ester (IV; $n = 2$), yielding the required protected octapeptide (I; $n = 6$). The products obtained by the two methods were identical, but the second method was preferred as being more economical.

As in the earlier work,[3] the protected peptides (I; $n = 5$ and 6) were reduced with an alkali metal in liquid ammonia, and the resulting cysteinyl-polyglycyl-cysteines (II; $n = 5$ and 6) were oxidised in aqueous solution, at a concentration of 0·5% and a pH of 8·6; since, however, we wished to isolate the oxidation products the earlier technique required modification. Further work [1,18] having shown the course of the oxidation of cysteinyl-tetraglycyl-cysteine to be markedly affected by traces of metal ions, the reductions were carried out in redistilled ammonia in an apparatus (Fig. 1) designed to allow the oxidation to be carried out in the vessel used for the prior removal of the protecting groups.

In view of the relative inaccessibility of the dicysteine peptides, exploratory experiments were carried out with the more easily available *N*-benzyloxycarbonyldiglycyl-*S*-benzyl-L-cysteine benzyl ester (VI). This was reduced, in liquid ammonia, with either lithium or potassium, to diglycyl-L-cysteine which was then oxidised as usual. Attempts to purify

(VI) Z·[NH·CH$_2$·CO]$_2$·NH·CH(CH$_2$·S·CH$_2$Ph)·CO$_2$·CH$_2$Ph (H·[NH·CH$_2$·CO]$_2$·NH·CH(CO$_2$H)·CH$_2$·S·)$_2$ (VII)

the product from the lithium reduction by extraction of the lithium salts with ethanol were unsuccessful, but it proved possible to isolate the oxidation product, bisdiglycyl-L-cystine (VII) by use of an ion-exchange resin; the bis-2,4-dinitrophenyl derivative was also isolated in satisfactory yield. A satisfactory experimental procedure having been thus established, attention was turned to the dicysteine peptides.

The protected hepta- and octa-peptides (I; $n = 5$ and 6) were reduced with sodium in liquid ammonia, and the resulting L-cysteinyl-penta- and -hexa-glycyl-L-cysteine (II;

[17] Ben-Ishai and Berger, *J. Org. Chem.*, 1952, **17**, 1564.
[18] Large, Ph.D. Thesis, Manchester, 1959.

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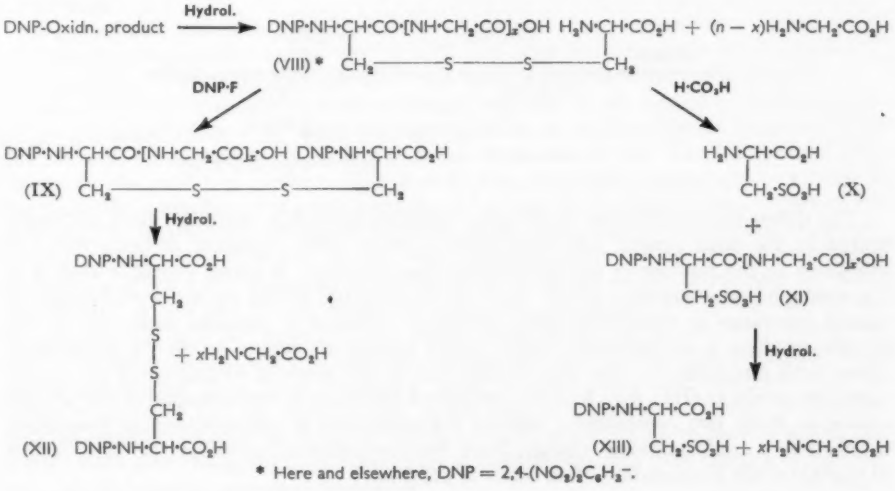
$n = 5$ and 6) were then oxidised, as usual, by passing oxygen through 0·5% aqueous solutions at pH 8·6. Paper chromatography revealed the presence in the oxidation solutions of only one product in each case, but paper electrophoresis showed this to be contaminated by a small amount of a second product; in each case, both the major and the minor products contained free amino-groups and disulphide linkages. It is noteworthy that a similar minor product accompanied the major product (bisdiglycyl-L-cystine) of the oxidation of diglycyl-L-cysteine and it seems likely that all the minor products are diastereoisomerides of the major products, arising from the occurrence of a little racemisation during the synthesis of the protected peptides. The simplicity of the oxidation products of the hepta- and the octa-peptide (II; $n = 5$ and 6) is in marked contrast to the complexity of the mixtures resulting from the oxidation of the analogous lower peptides (II; $n = 0$—3).[3]

Although the use of an ion-exchange resin had proved successful in the isolation of the oxidation product of diglycyl-cysteine, it was thought inadvisable, owing to the possibility of disulphide interchange, to use such a procedure for isolating the oxidation products of the dicysteine peptides. Accordingly, salt-free aqueous solutions of the free peptides (II; $n = 5$ and 6) were prepared from the protected peptides by way of the mercury derivatives, du Vigneaud and Miller's general procedure[19] being used. The oxidation products were precipitated, by addition of ethanol to the concentrated oxidised solutions, as white, hygroscopic powders, contaminated by small amounts (3—4%) of barium sulphate; in both cases the chromatographic and the electrophoretic behaviour of the products (isolated in about 50% yield) were the same as those of the major component of the corresponding crude oxidation mixture. Treatment of the oxidation products with 1-fluoro-2,4-dinitrobenzene in aqueous-ethanolic sodium carbonate gave the chromatographically homogeneous *N*-2,4-dinitrophenyl derivatives; as in the work of Heaton, Rydon, and Schofield,[3] the structures of the oxidation products were determined by studying the partial acid-hydrolyses of these derivatives.

The *N*-2,4-dinitrophenyl derivative of the oxidation product of cysteinyl-pentaglycyl-cysteine was heated with a mixture of acetic and hydrochloric acid, samples being removed



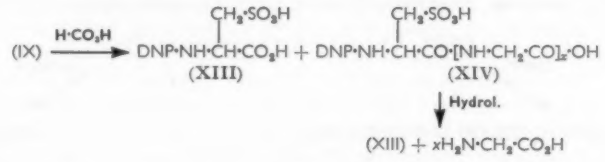
* Here and elsewhere, DNP = $2,4\text{-}(NO_2)_2C_6H_3^-$.

for chromatography from time to time; the progress of the hydrolysis is represented in Fig. 2. An initial hydrolysis product, *A*, yellow and ninhydrin-positive, appeared after

[19] du Vigneaud and Miller, *Biochem. Preps.*, 1952, **2**, 87.

10 min.; as the hydrolysis proceeded, the spot corresponding to this product developed into a streak and spots corresponding to glycine, cystine, and the mono- and bis-*N*-2,4-dinitrophenyl derivatives of the latter appeared. A further quantity of the *N*-2,4-dinitrophenyl derivative of the oxidation product was hydrolysed for 15 min. and the initial hydrolysis product, *A*, was isolated by elution from paper chromatograms. Oxidation of *A* with performic acid [20] gave cysteic acid (X) and a yellow, ninhydrin-negative product, *B*, which, on complete acid hydrolysis gave only glycine and *N*-2,4-dinitrophenylcysteic acid (XIII). It follows that the initial hydrolysis product, *A*, has the structure (VIII), the oxidation product, *B*, being the derived cysteic acid peptide (XI); the course of the degradation is shown in the chart. The presence of a free amino-group in the initial hydrolysis product (VIII) was confirmed by the observation that treatment with 1-fluoro-2,4-dinitrobenzene gave a new product (IX), yellow and ninhydrin-negative, which on complete hydrolysis yielded glycine and bis-*N*-2,4-dinitrophenylcystine (XII).

The *N*-2,4-dinitrophenyl derivative of the oxidation product of cysteinyl-hexaglycyl-cysteine was subjected to progressive hydrolysis in similar fashion to that used with the pentaglycyl compound; the relevant chromatogram is shown in Fig. 3. The pattern was similar to that observed with the heptapeptide, except that the initial hydrolysis product, *C*, gave no obvious reaction with ninhydrin and neither cystine nor its dinitrophenyl derivatives appeared to be formed. Nevertheless, the chemical behaviour of the initial hydrolysis product, *C*, was very similar to that of the product similarly obtained from cysteinyl-pentaglycyl-cysteine; oxidation of *C* gave cysteic acid (X) and a yellow, ninhydrin-negative product (XI), which yielded *N*-2,4-dinitrophenylcysteic acid (XIII) and glycine on complete hydrolysis. The presence of a free amino-group in *C*, despite its failure to react visibly with ninhydrin, was established by treating it with 1-fluoro-2,4-dinitrobenzene, which converted it into another yellow compound, *D*. Oxidation of this compound *D* with performic acid gave 2,4-dinitrophenylcysteic acid and a yellow, ninhydrin-negative product, *E*, which gave 2,4-dinitrophenylcysteic acid and glycine on complete hydrolysis. These observations show that *C*, like *A*, must be represented by (VIII), *D* and *E* being (IX) and (XIV), respectively, thus:



The difference in behaviour of *A* and *C* towards ninhydrin, although both are represented by the same general structure (VIII), is most easily explained as being due to a difference in the number of glycine residues they contain; it seems probable that *A* is the monoglycine compound (VIII; $x = 1$), encountered in the earlier work,[3] which it closely resembles in chromatographic behaviour, whereas *C* contains more (up to six) glycine residues, a circumstance which would explain its failure to give a pronounced colour with ninhydrin.[21] The implied difference in the mode of hydrolysis of the parent oxidation products (III; $n = 5$ and 6) indicates a difference in conformation of the peptide chains in these two compounds; abrupt discontinuities in physicochemical properties, ascribed to a conformational change, have been encountered at about the same length of peptide chain in ascending other series of peptides.[22]

[20] Sanger, *Nature*, 1947, **160**, 295; *Biochem. J.*, 1949, **44**, 126.
[21] Rydon and Smith, *Nature*, 1952, **169**, 922.
[22] Cf., *inter alia*, Idelson and Blout, *J. Amer. Chem. Soc.*, 1957, **79**, 3948; Mitchell, Woodward, and Doty, *ibid.*, p. 3955; Goodman and Schmitt, *ibid.*, 1959, **81**, 5507.

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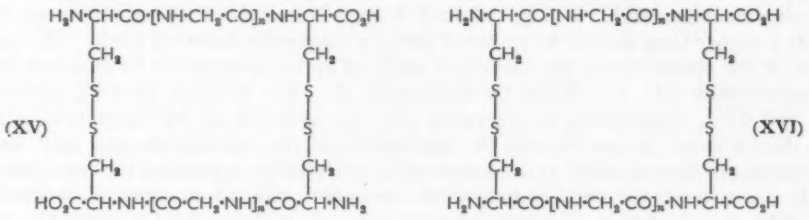
The structure (VIII) assigned to the initial hydrolysis products of the *N*-2,4-dinitrophenyl derivatives of the oxidation products of cysteinyl-pentaglycyl- and -hexaglycyl-cysteine shows that the oxidation products themselves must be the cyclic monomers (III),



the anti-parallel dimers (XV), or higher, anti-parallel, polymers; parallel structures, such as (XVI), are definitely excluded since these would necessarily give rise to a mixture of a bisdinitrophenyl derivative and a compound containing no dinitrophenyl groups as the initial products of hydrolysis.

The chromatographic behaviour of the *N*-2,4-dinitrophenyl derivatives of the two oxidation products suggests strongly that these are, indeed, monomeric; the derivatives have R_F values of 0·37 and 0·35, respectively, in butanol–pyridine–water, whereas the corresponding derivatives of dimers, such as (XV), would be expected to have much lower R_F values.[3] Conclusive evidence in favour of the monomeric structure (III) for both oxidation products was obtained by partial dinitrophenylation.[23] On treatment with a deficiency of 1-fluoro-2,4-dinitrobenzene both oxidation products gave, in addition to unchanged starting material, only one yellow, dinitrophenylated product. This is to be expected on the basis of the monomeric structure (III), which contains only one amino-group, whereas a dimer such as (XV), containing two amino-groups, would be expected to give two yellow products (the mono- and the bis-dinitrophenyl derivative) in addition to unchanged starting material, as bisdiglycyl-cystine (VII) was shown to do in a control experiment.

We conclude, therefore, that, under the conditions of our experiments, oxidation of L-cysteinyl-pentaglycyl-L-cysteine (II; $n = 5$) and L-cysteinyl-hexaglycyl-L-cysteine (II; $n = 6$) gives, as almost the only products, the cyclic disulphides (III; $n = 5$ and 6).

This conclusion is similar to that previously reached [3] in the case of L-cysteinyl-tetraglycyl-L-cysteine (II; $n = 4$), which was likewise shown to yield mainly the cyclic monomer (III; $n = 4$) on oxidation; it is clear that the circumstance that the 20-membered ring present in the oxidation product (III; $n = 4$) from L-cysteinyl-tetraglycyl-L-cysteine is also found in a number of peptide hormones [5-7] is not attributable to any tendency for such rings to be formed more easily than the 23- and 26-membered disulphide rings encountered in the present work. It was very noticeable that the amount of by-product accompanying the cyclic monomer in the oxidation products of the hepta- and the octapeptide (II; $n = 5$ and 6) was much less than that encountered [1,18] in the case of the hexapeptide (II; $n = 4$); others [24] have noted the instability of 20-membered disulphide rings in aqueous solution and it is tempting to speculate that the fact that disulphide rings of this size, rather than those containing fewer or more amino-acid residues, occur in insulin,[5] oxytocin,[6] and the vasopressins [7] is not without significance. Rings of this size may be optimal in being the smallest which are sufficiently stable to have a useful life in body fluids while being the largest which are sufficiently reactive to be capable of reaction with suitable receptor groups in proteins.[25]

[23] Cf. Battersby and Craig, *J. Amer. Chem. Soc.*, 1951, **73**, 1887.
[24] Ressler, *Science*, 1958, **128**, 1281; Bodanszky and du Vigneaud, *J. Amer. Chem. Soc.*, 1959, **81**, 2504.
[25] Cf. Fong, Schwartz, Popenoe, Silver, and Schoessler, *J. Amer. Chem. Soc.*, 1959, **81**, 2592.

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Neither of the two cyclic disulphides (III; $n = 5$ and 6) exhibited avian depressor activity in the chicken or pressor activity in the rat, and neither inhibited the actions of oxytocin or vasopressin.

Approximate statistical calculations [26] have shown that the yield (90% in 1% solution) of cyclic monomer (III; $n = 4$) obtained from L-cysteinyl-tetraglycyl-L-cysteine (II; $n = 4$) is higher than that to be expected (58%) on a purely statistical basis. The same is true of the present cases, the calculated yields of cyclic monomer to be expected from the heptapeptide (II; $n = 5$) and the octapeptide (II; $n = 6$) being, for 0·5% solutions, 67% and 61%, respectively, as compared with the observed all but theoretical yields. Such discrepancies are not beyond the uncertainty of the calculations, and only direct experiment can show whether, as the number of glycine residues separating the two cysteines in (II) is increased, the yield of monomeric disulphide will fall as expected or whether some other factor, such as hydrogen-bonding within the peptide chain, is involved; such experiments are now in progress in these laboratories.

The optical rotatory powers of the known *SS'*-dehydro-L-cysteinyl-polyglycyl-L-cysteines (III) are collected in the following Table:

n in (III)	0	4	5	6	7
$[\alpha]_D$	−29° (N-HCl)	−25° (H_2O)	−4·5° (H_2O)	−4·3° (H_2O)	−1·4° (H_2O)
Reference	27	9	Present work	Present work	10

The fall in rotatory power in passing from the tetraglycyl to the pentaglycyl compound is very marked and must be connected with a conformational change. Inspection of models shows that, as the number of glycine residues in (III) increases, the number of possible conformations with the peptide linkages having the preferred *trans*-configuration [28] increases; the small rotatory powers of the compounds containing five or more glycine residues may be due either to their being able to take up a preferred conformation in which the individual contributions of the two cysteine residues to the optical rotatory power very nearly cancel one another out, or to the increased flexibility of the molecules and the consequent multiplication of optically cancelling conformations.[29]

Experimental

Optical rotations were measured in 2 dm. tubes (estimated error ±0·01°).

Paper chromatograms were run on Whatman No. 2 paper using the following solvent systems and conditions: *A*, Butan-1-ol–pyridine–water (2 : 1 : 2), equilibrated for 7 days; descending development. *B*, Butanol–acetic acid–water (1500 : 250 : 564), equilibrated for 4 weeks; descending development. *C*, Acetone–urea–water (60 : 0·5 : 40); [30] ascending development.

Paper electrophoresis was carried out on Whatman No. 2 paper in a horizontal and a vertical apparatus; distances moved from the origin towards the cathode are designated as + and towards the anode −. The following experimental conditions were used: *K*, Vertical; 0·5N-acetic acid (pH 2·8); 650 v; 2 hr. *L*, Vertical; borate buffer (pH 9·3); [31] 650 v; 1 hr. *M*, Horizontal; 0·5N-acetic acid; 600 v; 2 hr. *N*, Horizontal; borate buffer (pH 9·4); [31] 250 v; 2 hr.

Spots were revealed with ninhydrin, chlorine–starch–iodine [21] or nitroprusside, with or without added cyanide.[32]

S-Benzyl-L-cysteine, m. p. 212—214°, $[\alpha]_D^{23·5}$ +26·8° (*c* 1·0 in N-NaOH), was prepared by the method of Wood and du Vigneaud [33] in an average yield of 73% and converted (64—83%

[26] Rydon, Ciba Foundation Symposium on Amino-acids and Peptides with Antimetabolic Activity, 1958, p. 200; cf. Boissonnas and Schumann, *Helv. Chim. Acta*, 1952, **35**, 2229.
[27] Wade, Winitz, and Greenstein, *J. Amer. Chem. Soc.*, 1956, **78**, 373.
[28] Pauling, Corey, and Branson, *Proc. Nat. Acad. Sci.*, 1951, **37**, 205.
[29] Cf. Brewster, *J. Amer. Chem. Soc.*, 1959, **81**, 5483.
[30] Bentley and Whitehead, *Biochem. J.*, 1950, **46**, 341.
[31] Britton, "Hydrogen Ions," Chapman and Hall Ltd., London, 4th edn., 1955, Vol. I, p. 363.
[32] Toennies and Kolb, *Analyt. Chem.*, 1951, **23**, 823.
[33] Wood and du Vigneaud, *J. Biol. Chem.*, 1939, **130**, 109.

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yield) into the benzyl ester toluene-*p*-sulphonate, m. p. 158—159°, $[\alpha]_D^{18}$ −22·0° (*c* 1·0 in 90% EtOH), as described by Hooper *et al.*[2] and into the *N*-benzyloxycarbonyl derivative (70—95% yield), m. p. 97—98°, $[\alpha]_D^{19}$ −44·5° (*c* 1·0 in EtOAc), as described by Harington and Mead.[34]

Synthesis of Protected L-*Cysteinyl-pentaglycyl-*L-*cysteine* (with J. A. Schofield).

S-*Benzyl-*N-*benzyloxycarbonyl-*L-*cysteinyl-diglycyl-glycine Ether Ester* (IV; $n = 3$).—*S*-Benzyl-*N*-benzyloxycarbonyl-L-cysteine (3·45 g.) and diglycyl-glycine ethyl ester hydrochloride[35] (2·54 g.) in anhydrous pyridine (8 ml.) were treated with di-*o*-phenylene pyrophosphite[36] (3·5 g.) in a flask fitted with a calcium chloride guard-tube. After the contents had been swirled for 5 min., the flask was heated on a boiling-water bath for 45 min. After cooling, ice and water (200 g.) were added and the mixture was kept overnight at 0°. The precipitate was collected by filtration and washed (slurrying) successively with half-saturated sodium hydrogen carbonate solution (200 ml.), N-hydrochloric acid (100 ml.), and water (100 ml.). The dried product (3·4 g., 63%), m. p. 118·5—120·5°, was recrystallised from chloroform–ether, giving the required ester (2·58 g.; 47%), m. p. 124·5—126°, $[\alpha]_D^{21·5}$ −23·8° (*c* 1·0 in dioxan) (Found: N, 10·3. Calc. for $C_{26}H_{32}N_4O_7S$: N, 10·3%); other preparations gave yields of 39% and 45%.

The method of Hooper *et al.*[2] gave higher yields (62—65%) but the product, m. p. 125—127°, was partially racemised, $[\alpha]_D^{26}$ −17·7° (*c* 4·7 in dioxan); Hooper *et al.*[2] record m. p. 120°, $[\alpha]_D^{20}$ −2·2° (*c* 4·6 in dioxan), and their material was obviously extensively racemised.

*Diglycyl-*S-*benzyl-*L-*cysteine Benzyl Ester* (V; $n = 2$; R = H).—*N*-Benzyloxycarbonyl-diglycyl-*S*-benzyl-L-cysteine benzyl ester, prepared as described by Crofts *et al.*[12] in 75—92% yield, had m. p. 113·5—114·5°, $[\alpha]_D^{22}$ −34·1° (*c* 1·0 in 50% aqueous pyridine); the yield obtained by a mixed anhydride coupling of *N*-benzyloxycarbonyl-glycyl-glycine[37] and *S*-benzyl-L-cysteine benzyl ester, by means of ethyl chloroformate and triethylamine in chloroform, was only 49%.

This ester (2·25 g.) was kept at room temperature with a solution of dry hydrogen bromide (4·1 g.) in acetic acid (25 ml.). After 1 hr., anhydrous ether (150—200 ml.) was added and the precipitate collected after 40 min. Recrystallisation from ethanol–ether afforded *diglycyl-*S-*benzyl-*L-*cysteine benzyl ester hydrobromide* (1·0 g., 49%), m. p. 147—148°, $[\alpha]_D^{14}$ −38·0° (*c* 1·0 in 50% aqueous pyridine), $[\alpha]_D^{16·5}$ −39·3° (*c* 1·0 in H_2O), chromatographically homogeneous (R_F 0·58 in system *A*) (Found: C, 50·6, 50·4; H, 5·4, 5·3; N, 8·6. $C_{21}H_{26}BrN_3O_4S$ requires C, 50·8; H, 5·3; N, 8·5%); other preparations gave yields varying from 51 to 78%.

S-*Benzyl-*N-*benzyloxycarbonyl-*L-*cysteinyl-pentaglycyl-*S-*benzyl-*L-*cysteine Benzyl Ester* (I; $n = 5$).—*S*-Benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-diglycyl-glycine ethyl ester (2·93 g.) was added to hot ethanol (70 ml.) containing hydrazine hydrate (3·8 ml.); the mixture was shaken vigorously and then left to cool overnight. The precipitated hydrazide (2·57 g., 90%), m. p. 180—185°, was recrystallised from aqueous ethanol, affording the pure compound (2·2 g., 76%), m. p. 184·5—186°, $[\alpha]_D^{19}$ −27·8° (*c* 1·0 in 50% aqueous pyridine) (Found: C, 53·6; H, 5·7; N, 15·2. Calc. for $C_{24}H_{30}N_6O_6S$: C, 54·3; H, 5·7; N, 15·8%) (Hooper *et al.*[2] record m. p. 196°).

This hydrazide (2·65 g.) was dissolved by gentle warming in 80% acetic acid (80 ml.); the solution was cooled in ice and treated with ice-cold concentrated hydrochloric acid (5 ml.), followed by ice-cold 10% sodium nitrite solution (4 ml.). The azide formed was extracted into chloroform and the extract washed thrice with saturated sodium hydrogen carbonate solution and then dried (Na_2SO_4), the temperature being kept below 5° throughout. At the same time, a chloroform solution of diglycyl-*S*-benzyl-L-cysteine benzyl ester was prepared by dissolving the hydrobromide (2·48 g.) in a little water, adding chloroform (140 ml.) and triethylamine (1·6 ml.), and then, finally, shaking with sufficient anhydrous potassium carbonate to absorb all the water; the solution was then dried (Na_2SO_4). The two filtered chloroform solutions were mixed at 0° and the mixture was allowed to warm to room temperature overnight. Most of the chloroform was removed from the resulting gel under reduced pressure and the residue was then treated with ether. The resulting off-white solid (4·35 g., 95%) was collected and recrystallised, once from aqueous pyridine and once from aqueous ethanol, affording the fully protected heptapeptide (I; $n = 5$) (2·27 g., 50%), m. p. 225—226° (decomp.),

[34] Harington and Mead, *Biochem. J.*, 1936, **30**, 1598.
[35] Cook and Levy, *J.*, 1950, 646.
[36] Crofts, Markes, and Rydon, *J.*, 1958, 4250.
[37] Bergmann and Zervas, *Ber.*, 1932, **65**, 1192.

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$[\alpha]_D^{17}$ −32·5° (*c* 0·5 in 50% aqueous pyridine), $[\alpha]_D^{22}$ −25·3° (*c* 0·6 in acetic acid) (Found: C, 58·7; H, 5·8; N, 10·9. Calc. for $C_{45}H_{51}N_7O_{10}S_2$: C, 59·1; H, 5·6; N, 10·7%); Lautsch and Kraege [4] give m. p. 224—225°, $[\alpha]_D^{23}$ −27·2° (*c* 1·0 in acetic acid), for material synthesised by a different route. In eight other preparations the yield varied from 33 to 61%.

Synthesis of Protected L-*Cysteinyl-hexaglycyl-*L-*cysteine.*

Derivatives of S-*Benzyl-*N-*benzyloxycarbonyl-*L-*cysteinyl-triglycyl-glycine.*—*S*-Benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-glycyl-glycine ether ester (IV; $n = 2$), prepared in 85% yield by the method of Crofts *et al.*,[12] had m. p. 112—114°, $[\alpha]_D^{20}$ −13·5° (*c* 2·0 in EtOH); a much poorer yield (40%) was obtained by coupling *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteine and glycyl-glycine ethyl ester with the aid of dicyclohexylcarbodi-imide in chloroform or methylene chloride. This ester was converted into the hydrazide, m. p. 163—164°, $[\alpha]_D^{18}$ −29·4° (*c* 1·0 in 50% aqueous pyridine), after recrystallisation from aqueous ethanol, in 55% yield as described by Hooper *et al.*,[2] who record m. p. 164° but give no optical rotation.

This hydrazide (2·07 g.) was dissolved in warm 50% acetic acid (60 ml.), and treated at 0° with concentrated hydrochloric acid (7 ml.), followed by 10% aqueous sodium nitrite (5 ml.). The azide formed was extracted with chloroform, washed thrice with saturated sodium hydrogen carbonate solution, and dried (Na_2SO_4), at <5° throughout. At the same time, a chloroform solution of glycyl-glycine ethyl ester was prepared as usual from the hydrochloride (0·86 g.) and triethylamine. The filtered chloroform solutions were mixed at 0° and allowed to attain room temperature overnight. Working up as usual and recrystallisation from aqueous ethanol gave the *ethyl ester* (IV; $n = 4$) (2·0 g., 76%), m. p. 159—161°, $[\alpha]_D^{18}$ −28·9° (*c* 0·5 in 50% aqueous pyridine) (Found: C, 56·7; H, 6·5; N, 11·6. $C_{28}H_{35}N_5O_8S$ requires C, 55·9; H, 5·9; N, 11·6%). This ester (1·1 g.) was treated in hot ethanol (50 ml.) with hydrazine hydrate (2 ml.); after the mixture had cooled overnight, the precipitate (0·9 g., 84%), m. p. 187—190°, was recrystallised from methanol and from ethylene glycol, affording the *hydrazide* (0·61 g., 57%), m. p. 209—211° (Found: C, 52·5; H, 5·6. $C_{26}H_{33}N_7O_7S$ requires C, 53·1; H, 5·7%).

*Derivatives of Tetraglycyl-*S-*benzyl-*L-*cysteine.*—*N*-Benzyloxycarbonyl-glycyl-glycine [37] (2·66 g.) and diglycyl-*S*-benzyl-L-cysteine benzyl ester hydrobromide (4·96 g.) in anhydrous pyridine (20 ml.) were treated with di-*o*-phenylene pyrophosphite [36] (3·5 g.). The mixture was swirled for 5 min. and then heated on a boiling-water bath for 40 min. with intermittent shaking. Working up as usual, followed by recrystallisation from, successively, aqueous ethanol, aqueous acetone, and aqueous dimethylformamide, gave the *N*-benzyloxycarbonyl benzyl ester (3·95 g., 60%), m. p. 216—217°, $[\alpha]_D^{20}$ −24·6° (*c* 1·0 in acetic acid) (Found: N, 10·9. Calc. for $C_{33}H_{37}N_5O_8S$: N, 10·6%); Lautsch and Kraege [4] give m. p. 217—218·5°, $[\alpha]_D^{23}$ −24·5°, for material synthesised by a different route. In subsequent preparations the yields ranged from 62 to 77%.

This compound (1·0 g.) was kept for 1 hr. at room temperature, with occasional shaking, with a solution of dry hydrogen bromide (2·8 g.) in acetic acid (17 ml.); anhydrous ether (200 ml.) was then added and the mixture set aside overnight. Collection of the precipitate and recrystallisation from ethanol–ether gave the *benzyl ester hydrobromide* (0·57 g., 53%), m. p. 152—154° (Found: N, 11·9. $C_{25}H_{32}BrN_5O_6S$ requires N, 11·5%), chromatographically homogeneous (R_F 0·41 in system *A*).

S-*Benzyl-*N-*benzyloxycarbonyl-*L-*cysteinyl-hexaglycyl-*S-*benzyl-*L-*cysteine Benzyl Ester* (I; $n = 6$).—(*a*)Tetraglycyl-*S*-benzyl-L-cysteine benzyl ester hydrobromide (1·0 g.) was dissolved in warm water (15 ml.), and the solution mixed with ethyl acetate (60 ml.). Triethylamine (2·5 ml.) was added, followed by sufficient anhydrous potassium carbonate to absorb the water; the ethyl acetate layer was then separated and dried (Na_2SO_4). At the same time, *S*-benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-glycyl-glycine hydrazide (0·8 g.) was dissolved in warm 50% acetic acid (14 ml.) and treated at 0° with ice-cold concentrated hydrochloric acid (4 ml.), followed by ice-cold 10% aqueous sodium nitrite (3 ml.); the azide was extracted with ethyl acetate, washed thrice with saturated sodium hydrogen carbonate solution, and dried (Na_2SO_4), at <5° throughout. The two filtered ethyl acetate solutions were mixed at 0° and allowed to attain room temperature overnight. The solvent was then removed under reduced pressure and the residue twice recrystallised from acetic acid (charcoal), giving the protected *octapeptide* (0·68 g., 45%), m. p. 244—246° (decomp.), $[\alpha]_D^{22}$ −30·3° (*c* 0·4 in 50% aqueous pyridine), $[\alpha]_D^{21}$ −20·7° (*c* 0·6 in acetic acid) (Found: C, 57·9; H, 5·9; N, 10·6. $C_{47}H_{54}N_8O_{11}S_2$ requires C, 58·1; H, 5·6; N, 11·5%); Lautsch *et al.*[8] give m. p. 258—260°, $[\alpha]_D$ −25·7° (in acetic acid)

for material synthesised by a different route but record no analysis. In further preparations, chloroform was found to be as good as ethyl acetate as solvent for this coupling, and ether to be much inferior; the yields obtained varied from 35 to 61%.

(*b*) *S*-Benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-triglycyl-glycine azide (from the hydrazide, 0·85 g.) and diglycyl-*S*-benzyl-L-cysteine benzyl ester (from the hydrobromide, 0·72 g.) were coupled, as usual, in chloroform. Recrystallisation of the crude product (0·94 g., 67%) from aqueous pyridine gave the same protected octapeptide, m. p. 246—247° (decomp.) (Found: N, 11·2%).

Oxidations.

Removal of the protecting groups from the protected peptides and oxidation of the resulting cysteine peptides were carried out in the apparatus shown in Fig. 1, consisting of a flat-bottomed cylindrical vessel fitted with a gas inlet tube *A* and a side-arm *B* and provided with two externally-fitting ground glass caps (B40 joints), one (*C*) provided with a stirrer guide, the other (*D*) being a simple cap.

The protected peptide was dissolved in liquid ammonia in the reaction vessel, fitted with *C* and a stirrer, tap *A* being closed and *B* fitted with a soda-lime guard tube. Small pieces of alkali metal were added, with stirring, until a blue colour was stable for 15 min. Ammonium chloride equivalent to the amount of alkali metal used in excess of the amount required to form the alkali-metal salt of the cysteine peptide was added, with stirring, and the cap *C* replaced by cap *D*. The ammonia was then allowed to evaporate, initially at atmospheric pressure and then for 2—3 hr. at 0·1 mm. The vessel was then filled, through *A*, with nitrogen, and a current of nitrogen passed through the apparatus while boiled-out distilled water was added to dissolve the alkali-metal salt of the cysteine peptide. The pH was then brought to 8·6 with 2N-hydrochloric acid, and the volume finally made up with boiled-out distilled water to give the desired (usually 0·5%) concentration of the peptide. Oxygen was then passed through the solution at about 500 ml./min. until oxidation was complete (negative nitroprusside reaction). The resulting solution was extracted with ether, evaporated almost to dryness under reduced pressure, brought to pH 5 with hydrochloric acid, and then evaporated to dryness under reduced pressure at room temperature and finally over calcium chloride or phosphorus pentoxide in a vacuum-desiccator.

Oxidation of Diglycyl-L-cysteine.—(*a*) *N*-Benzyloxycarbonyldiglycyl-*S*-benzyl-L-cysteine benzyl ester (1·2 g.) was reduced with potassium in liquid ammonia (50 ml.), and the resulting diglycyl-L-cysteine oxidised in water (100 ml.) at pH 8·6 (6·5 hr.).

Paper chromatography showed only one, ninhydrin-positive, product, having R_F 0·04 in system *A* and R_F 0·00 in system *B*. Paper electrophoresis showed the main oxidation product to be accompanied by a small amount of another product, thus:

Conditions (see p. 1758)	*K*	*L*	*M*
Movement of major component (cm.)	+9·5	−3·5	+14·0
Movement of minor component (cm.)	+12·0	−2·5	+18·5

(*b*) The product of another reduction was dissolved in water (100 ml.) and run through a column (3 × 19 cm.) of Zeo-Karb 225 ion-exchange resin; water was then run through the column until the effluent was free from chloride ions. The peptide was then eluted with 0·2N-ammonia, and the eluate evaporated to dryness under reduced pressure. The residue was dissolved in water (30 ml.) and again evaporated to dryness. Six such treatments gave a product (0·25 g., 24%) which was free from ammonium and potassium ions; a specimen, recrystallised from acetic acid–ether and dried at 80°, had m. p. 190—200° (decomp.) and was shown by analysis to be *bisdiglycyl-L-cystine dihydrate* (Found: C, 33·3; H, 6·3; N, 15·9. $C_{14}H_{24}N_6O_8S_2,2H_2O$ requires C, 33·3; H, 5·6; N, 16·7%).

(*c*) The product from another experiment was dissolved in water (15 ml.), containing sodium hydrogen carbonate (1·0 g.), and shaken for 5 hr. with 1-fluoro-2,4-dinitrobenzene (0·9 ml.) in ethanol (20 ml.); a further 0·3 ml. of fluorodinitrobenzene was then added and the mixture shaken for a further 3 hr. The mixture was then extracted repeatedly with ether, and the residual solution acidified. Recrystallisation of the precipitate, first from aqueous methanol and then from acetic acid, gave *bis*-(N-2,4-*dinitrophenyldiglycyl*)-L-*cystine*, m. p. 174—176° (decomp.) (Found: C, 38·3; H, 3·8; N, 16·8. $C_{26}H_{28}N_{10}O_{16}S_2$ requires C, 39·0; H, 3·5; N, 17·5%), chromatographically homogeneous (R_F 0·38 in system *A*).

Oxidation of L-*Cysteinyl-pentaglycyl*-L-*cysteine.*—(*a*) *S*-Benzyl-$^{I}_{t}$*N*-benzyloxycarbonyl-L-cysteinyl-pentaglycyl-*S*-benzyl-L-cysteine benzyl ester (0·9 g.) was reduced with sodium (0·51 g.) in liquid ammonia (50 ml.), and the resulting L-cysteinyl-pentaglycyl-L-cysteine oxidised in water (100 ml.) at pH 8·6 (25 min.).

Paper chromatography revealed only one ninhydrin-positive product, appearing as a single, precisely defined, spot (R_F 0·78) in system *C* and as a single, tailed spot (R_F 0·13 and 0·02, respectively) in systems *A* and *B*. Paper electrophoresis revealed the major component accompanied by a small amount of a slower-moving product, thus:

Conditions	*M*	*N*
Movement of major component (cm.)	+13·0	−4·0
Movement of minor component (cm.)	+9·0	−1·5

(*b*) The protected heptapeptide (2·26 g.) was reduced with sodium in liquid ammonia (110 ml.). Excess of sodium was destroyed with ammonium sulphate, and the ammonia evaporated as usual. The residue was dissolved, under nitrogen, in 0·5N-sulphuric acid (120 ml.)

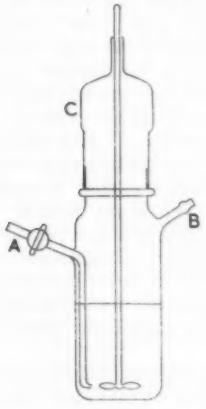

FIG. 1. *Apparatus for removal of protecting groups from protected dicysteine peptides and oxidation of the resulting free peptides.*

and treated with 20 ml. of an acid solution of mercuric sulphate, prepared by mixing mercuric sulphate (200 g.), 10N-sulphuric acid (500 ml.), concentrated sulphuric acid (40 ml.), and water (600 ml.) in the order stated. After 18 hr., the copious white precipitate was collected by centrifugation, washed thrice with 0·5N-sulphuric acid, and dried overnight in a vacuum (P_2O_5).

A brisk stream of hydrogen sulphide was passed through a suspension of the product (*ca.* 3 g.) in water (25 ml.) for 2·5 hr. with occasional shaking; mercuric sulphide was then removed by centrifugation and washed thrice with water. To the supernatant liquid and washings sulphuric acid was added to give a concentration of 0·5N. Nitrogen was passed through the solution for 3 hr. to remove hydrogen sulphide, after which the pH was brought to 8·6 with saturated barium hydroxide solution, and the precipitated barium sulphate removed. The filtrate and washings therefrom were made up to 280 ml. with boiled-out distilled water and oxygen passed through at 500 ml./min. until oxidation was complete (15 min.). The solution was concentrated under reduced pressure to 80 ml. and sulphuric acid added to remove all barium ions. The filtered solution was evaporated almost to dryness under reduced pressure and the residue treated with an excess of absolute ethanol. The precipitated SS′-*dehydro*-L-*cysteinyl-pentaglycyl*-L-*cysteine* (0·71 g., 57%), collected by centrifugation, washed with ethanol and ether, and dried to constant weight in a vacuum ($CaCl_2$), had m. p. 197—200° (decomp.), $[\alpha]_D^{21}$ −4·5° (*c* 0·4 in H_2O) (Found: C, 37·3; H, 5·1; N, 18·1; residue, 3·6. Corrected for residue: C, 38·7; H, 5·3; N, 18·8. $C_{16}H_{25}N_7O_8S_2$ requires C, 37·9; H, 5·0; N, 19·3%); paper electrophoresis (conditions *M* and *N*) gave patterns similar to those obtained with the oxidation product from experiment (*a*).

(*c*) In another experiment the oxidation product, from the protected heptapeptide (0·9 g.), was dissolved in 0·4N-sodium carbonate (25 ml.) and converted into the 2,4-dinitrophenyl

derivative as described for the oxidation product of diglycyl-cysteine. The product was freed from 2,4-dinitrophenol by extraction (Soxhlet) with ether; the resulting N-2,4-*dinitrophenyl*-SS′-*dehydro*-L-*cysteinyl-pentaglycyl*-L-*cysteine*, m. p. 190—196° (decomp.), was chromatographically homogeneous (R_F 0·37 in system *A*) and analysed as the *dihydrate* (Found: C, 37·3; H, 4·1; N, 17·7. $C_{22}H_{27}N_9O_{12}S_2,2H_2O$ requires C, 37·2; H, 4·4; N, 17·7%).

Oxidation of L-*Cysteinyl-hexaglycyl*-L-*cysteine*.—(*a*) *S*-Benzyl-*N*-benzyloxycarbonyl-L-cysteinyl-hexaglycyl-*S*-benzyl-L-cysteine benzyl ester (0·86 g.) was reduced and the product oxidised as described for the pentaglycyl compound; the final oxidation required 35 min. Paper chromatography showed the presence of only one product (R_F 0·08 in system *A* and 0·02 in system *B*), but paper electrophoresis (conditions *M*) showed the main product (migration + 12·0 cm.) to be accompanied by a small amount of a second product (migration + 8·0 cm.).

(*b*) The protected octapeptide (2·0 g.) was reduced and the product oxidised by the mercaptide procedure described above for the heptapeptide. The resulting SS′-*dehydro*-L-*cysteinyl-hexaglycyl*-L-*cysteine* (0·54 g., 47%) had m. p. 189—191° (decomp.), $[\alpha]_D^{20}$ −4·3° (*c* 0·5 in water), and analysed as the *monohydrate* (Found: C, 36·3; H, 5·5; N, 18·2; S, 10·6; residue, 3·0. Corrected for residue: C, 37·7; H, 5·7; N, 18·7; S, 11·7. $C_{18}H_{28}N_8O_9S_2,H_2O$ requires C, 37·1; H, 5·2; N, 19·2; S, 11·0%).

(*c*) In another experiment the oxidation product, without isolation, was converted as usual into the 2,4-dinitrophenyl derivative. The resulting N-2,4-*dinitrophenyl*-SS′-*dehydro*-L-*cysteinyl-hexaglycyl*-L-*cysteine*, m. p. 159—163° (decomp.), was chromatographically homogeneous (R_F 0·35 in system *A*) and analysed as the *monohydrate* (Found: C, 38·1; H, 3·7; N, 16·4. $C_{34}H_{30}N_{10}O_{13}S_2,H_2O$ requires C, 38·1; H, 3·7; N, 17·1%).

Partial Hydrolysis of Oxidation Products.

(a) *Dehydro-cysteinyl-pentaglycyl-cysteine*.—(i) The 2,4-dinitrophenyl derivative (10 mg.) was heated at 98° with a hydrolysis mixture (0·5 ml.) containing equal volumes of acetic acid and 20% hydrochloric acid; from time to time a little of the solution was spotted on paper. After addition of marker spots (glycine and the product of heating a mixture of L-cystine and its bis-*N*-2,4-dinitrophenyl derivative in the same hydrolysis mixture) the chromatogram was developed with solvent system *A*. After having been sprayed with ninhydrin and heated, the chromatogram had the appearance shown in Fig. 2; the markers are cystine (R_F 0·04), glycine (R_F 0·10), mono-*N*-2,4-dinitrophenylcystine (R_F 0·41), and bis-*N*-2,4-dinitrophenylcystine (R_F 0·60).

(ii) In another experiment, the 2,4-dinitrophenyl derivative (3 mg.) was heated for 15 min. at 98° with the same hydrolysis mixture (0·15 ml.). The solution was rapidly cooled and evaporated to dryness at room temperature; the residue was dissolved in a little dimethylformamide and applied as a band to a strip of filter paper. After development (system *A*), the band corresponding to the main product (R_F 0·38) was cut out and eluted with dimethylformamide. The eluate was evaporated to dryness under reduced pressure and the residue dissolved in 0·05 ml. of a solution of performic acid (from formic acid, 6 ml., and 20-vol. hydrogen peroxide, 1 ml.). After an hour the solution was evaporated to dryness under reduced pressure and the residue applied in dimethylformamide as a band to a strip of filter paper. Development with system *A* revealed the presence of cysteic acid (R_F 0·08; colourless and ninhydrin-positive) and a yellow, ninhydrin-negative substance (R_F 0·34). The latter was eluted with dimethylformamide and heated at 98° for 3·5 hr. with a few drops of the usual hydrolysis mixture. Chromatography (system *A*) showed the hydrolysate to contain only glycine (R_F 0·10; colourless and ninhydrin-positive) and *N*-2,4-dinitrophenylcysteic acid (R_F 0·38; yellow and ninhydrin-negative).

(iii) In a third experiment, the initial hydrolysis product, prepared as in (ii) from the *N*-2,4-dinitrophenyl derivative (5 mg.), was dissolved in 2% aqueous sodium hydrogen carbonate (0·5 ml.) and shaken mechanically for 4 hr. with 1-fluoro-2,4-dinitrobenzene (0·05 ml.) in a little ethanol. The solution was concentrated, extracted with ether, and acidified; the yellow precipitate, collected by centrifugation, was applied to paper in dimethylformamide, and the chromatogram was developed with system *A*. The main product (R_F 0·46; yellow and ninhydrin-negative), which was accompanied by a trace of 2,4-dinitrophenylglycine (R_F 0·66), was eluted with dimethylformamide and heated at 98° for 3 hr. with a few drops of the usual hydrolysis mixture. The only products detected in the hydrolysate by paper chromatography (system *A*) were glycine (R_F 0·10) and bis-*N*-2,4-dinitrophenylcystine (R_F 0·59).

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(b) *Dehydro-cysteinyl-hexaglycyl-cysteine.*—The procedures were the same as those used with the pentaglycyl compound; in the following, R_F values are all for system *A*.

(i) The paper chromatogram of the progressive hydrolysis of the 2,4-dinitrophenyl derivative had the appearance shown in Fig. 3.

(ii) Oxidation of the initial hydrolysis product (R_F 0·39) gave cysteic acid (R_F 0·08) and a yellow, ninhydrin-negative substance (R_F 0·34); hydrolysis of the latter gave only glycine (R_F 0·10) and *N*-2,4-dinitrophenylcysteic acid (R_F 0·38).

FIG. 2. *Chromatogram showing the effect of various periods of hydrolysis on the dinitrophenyl derivative of the oxidation product of* L-*cysteinyl-pentaglycyl-*L-*cysteine.*

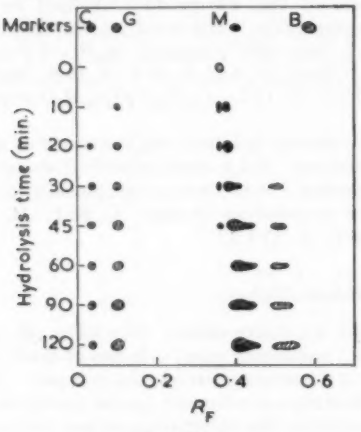
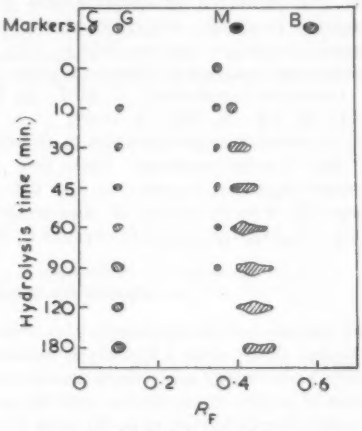


FIG. 3. *Chromatogram showing the effect of various periods of hydrolysis on the dinitrophenyl derivative of the oxidation product of* L-*cysteinyl-hexaglycyl-*L-*cysteine.*



//// *Yellow.* \\\\ *Ninhydrin positive.*

C = L-*Cystine.* G = *Glycine.* M = *Mono-N-2,4-dinitrophenyl-*L-*cystine.* B = *Bis-N-2,4-dinitrophenyl-*L-*cystine.*

(iii) Dinitrophenylation of the initial hydrolysis product (R_F 0·39) gave a yellow, ninhydrin-negative product (R_F 0·47) which, on oxidation with performic acid, gave *N*-2,4-dinitrophenylcysteic acid (R_F 0·38) and another yellow, ninhydrin-negative product (R_F 0·34). Hydrolysis of the latter gave only glycine (R_F 0·10) and *N*-2,4-dinitrophenylcysteic acid (R_F 0·38).

Partial Dinitrophenylation of Oxidation Products.

(a) *Bisdiglycyl-*L-*cystine.*—The crude oxidation product, from *N*-benzyloxycarbonyl-diglycyl-*S*-benzyl-L-cysteine benzyl ester (1·2 g.), was dissolved in water (15 ml.) containing sodium hydrogen carbonate (1 g.), and the solution shaken mechanically for 2 hr. with 1-fluoro-2,4-dinitrobenzene (0·23 ml., 0·85 equiv.) in ethanol (10 ml.). Ethanol was removed under reduced pressure and the residue diluted with water and extracted with ether. Paper chromatography of the residual solution (system *A*) showed three spots: (i) R_F 0·04; colourless, ninhydrin and cyanide–nitroprusside positive; bisdiglycyl-L-cystine. (ii) R_F 0·30; yellow, ninhydrin and cyanide–nitroprusside positive; mono-*N*-2,4-dinitrophenyl-diglycyl-L-cystine. (iii) R_F 0·39; yellow, ninhydrin negative, cyanide–nitroprusside positive; bis-*N*-2,4-dinitrophenyl-diglycyl-L-cystine.

(b) *Dehydro-cysteinyl-pentaglycyl-cysteine.*—The crude oxidation product, from the protected heptapeptide, (I; $n = 5$) (0·9 g.), was treated similarly with 1-fluoro-2,4-dinitrobenzene (0·08 g., 0·43 equiv.). Paper chromatography of the product (system *A*) showed the presence of only the dehydroheptapeptide (R_F 0·10; colourless; ninhydrin and cyanide–nitroprusside positive) and its *N*-2,4-dinitrophenyl derivative (R_F 0·37; yellow; ninhydrin negative and cyanide–nitroprusside positive).

(c) *Dehydro-cysteinyl-hexaglycyl-cysteine.*—A similar experiment with the protected octapeptide (I; $n = 6$) gave only the dehydro-octapeptide (R_F 0·06; colourless; ninhydrin and

cyanide–nitroprusside positive) and its *N*-2,4-dinitrophenyl derivative (R_F 0·35; yellow; ninhydrin-negative and cyanide–nitroprusside positive).

We thank the Department of Scientific and Industrial Research for the award of a Research Studentship (to D. J.) and Imperial Chemical Industries Limited for financial assistance. We are indebted to Professor V. du Vigneaud for permission to report the physiological tests, which were carried out in his laboratories at Cornell University Medical College by Miss Maureen O'Connell. The work described in this paper was begun in the Department of Chemistry, Manchester College of Science and Technology.

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342. *The Effect of Pressure on the First Acid Dissociation Constants of "Sulphurous" and Phosphoric Acids.*

By A. J. ELLIS and D. W. ANDERSON.

By means of conductance measurements at 25°, the changes with pressure of the first dissociation constants for "sulphurous" and phosphoric acids were determined up to 2000 atmospheres. The effect of pressure on the ionisation of the sulphur dioxide–water system is much less than for two other hydrated-gas systems, ammonia and carbon dioxide, but the effect is greater than for simple weak acids.

THE evidence available shows that in aqueous solutions of sulphur dioxide the un-ionized sulphur species consist mainly of uncombined sulphur dioxide molecules, with sulphurous acid (H_2SO_3) molecules, if present, in very minor amounts. The studies include Raman,[1,2] infrared,[3,4] and ultraviolet absorption [5] techniques.

The results from infrared spectra are the most convincing. Sulphur dioxide solutions in water show only the infrared absorption bands typical of SO_2 molecules in the liquid and the gaseous state. Even at −190° there is no evidence from infrared measurements for a SO_2–H_2O combination.[3]

This contrasts with the earlier results given by Maass *et al.*,[6,7] who attempted to calculate from vapour-pressure and conductance measurements the proportions of combined and uncombined sulphur dioxide in the system

$$SO_2(g) \rightleftharpoons SO_2(aq) \overset{K_1}{\rightleftharpoons} H_2SO_3 \overset{K_2}{\rightleftharpoons} H^+ + HSO_3^-$$

Their calculations have little quantitative significance owing to the neglect of activity corrections at high ionic strengths, and to incomplete information on the ionic conductance of the bisulphite ion.

More recently, De Maine [5] showed that the total un-ionized sulphur dioxide in aqueous solution has an extinction coefficient at 278 mμ very similar to that for sulphur dioxide dissolved in organic solvents and in the gas phase. From his spectrophotometric measurements he suggested that the system may be more complex than the simple three-step equilibrium outlined above, but his work is subject to the same criticisms as that of Maass *et al.*[6,7]

[1] Rao, *Proc. Indian Acad. Sci.*, 1944, *A*, **20**, 292.
[2] Simon and Waldmann, *Z. anorg. Chem.*, 1956, **283**, 359.
[3] Falk and Giguere, *Canad. J. Chem.*, 1958, **36**, 1121.
[4] Jones and McLaren, *J. Chem. Phys.*, 1958, **28**, 995.
[5] De Maine, *J. Chem. Phys.*, 1957, **26**, 1036, 1049.
[6] Boyd-Campbell and Maass, *Canad. J. Res.*, 1930, **2**, 42.
[7] Morgan and Maass, *Canad. J. Res.*, 1931, **5**, 162.

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The effects of pressure on ionization in the systems ammonia–water [8] and carbon dioxide–water [9] have been reported. We now compare the effects of pressure on the apparent first ionization constant for these two systems and for the sulphur dioxide–water system. Results are also presented for the first acid dissociation constant for phosphoric acid as a simple inorganic acid with a dissociation constant similar to the apparent dissociation constant of sulphurous acid. The effect of pressure on the ionization of acetic acid was redetermined as a check on the reproducibility of the high-pressure conductance method between workers.

Experimental

Materials and Apparatus.—Reagents used were of " AnalaR " quality and were not purified further. Sulphur dioxide solutions were prepared in bulk from B.D.H. liquid sulphur dioxide, and portions run quickly into the conductance cell. Potassium hydrogen sulphite solutions were made by adjusting sulphur dioxide solutions to pH 4·5 with potassium hydroxide solution. A pH meter was used.

The apparatus used was essentially the same as in the previous papers of this series.[9,10]

Method.—The methods of calculation and symbols are as given in a previous paper.[10] Published values of the conductances in water at high pressures for hydrochloric acid and potassium chloride [8] were used in conjunction with those given below for the acids and their potassium salts in order to derive K_a values. The necessary activity corrections were made at each ionic strength and pressure.

Table 1. *Values of* $\Lambda^P\rho_r/\Lambda^1$ *for potassium salts at 25° over a concentration range. (Values of* Λ^1 *for 0·01M-solutions in parentheses.)*

P (atm.)	1	500	1000	1500	2000
$KHSO_3$, 0·01—0·15M	(120)	1·031	1·052	1·062	1·065
KH_2PO_4, 0·002—0·1M	(99·2)	1·033	1·053	1·068	1·074
KOAc, 0·001—0·05M	(106)	1·026	1·042	1·045	1·048

Table 2. *Apparent acid dissociation constant* K_a ($\times 100$) *for " sulphurous acid " ($H_2O + SO_2$) at 25°.*

P (atm.)	1	500	1000	1500	2000
100 × Concn (M)					
1·17	1·39	2·0	3·1	4·6	6·4
1·80	1·44	2·1	3·0	4·7	6·2
2·32	1·40	2·1	3·1	4·6	6·5
6·35	1·40	2·1	3·2	4·7	6·2
9·7	1·33	2·0	3·0	4·4	6·2
23·4	1·39	2·0	3·0	4·5	6·4

$\Delta V^1 = -19·7$ c.c. mole^{-1}; $\Delta V^{2000} = -15·2$ c.c. mole^{-1}.
Average $\Delta K = -2·3 \times 10^{-3}$ atm.$^{-1}$ c.c. mole^{-1}.

Table 3. *First acid dissociation constant* K_a ($\times 100$) *for phosphoric acid at high pressures and 25°.*

P (atm.)	1	500	1000	1500	2000
Concn. (M)					
0·00576	0·71	0·98	1·33	1·69	2·10
0·01	0·67	0·90	1·20	1·55	2·01
0·1	0·88	1·21	1·64	2·12	2·55

$\Delta V^1 = -15·5$ c.c. mole^{-1}; $\Delta V^{2000} = -10·7$ c.c. mole^{-1}.
Average $\Delta K = -2·4 \times 10^{-3}$ atm.$^{-1}$ c.c. mole^{-1}.

Results.—Table 1 gives the conductance ratio results for the three potassium salts: Table 2 summarizes the results for sulphur dioxide ionization under pressure at 25°, and Table 3 gives similar information for phosphoric acid at 25°. Results from the present work and from other authors are compared for acetic acid in Table 4. V is the partial molar volume, and ΔK is the change in compressibility on ionisation.

[8] Hamann, " Physico-chemical Effects of Pressure," Butterworths, London, 1957.
[9] Ellis, *J.*, 1959, 3689.
[10] Clark and Ellis, *J.*, 1960, 247.

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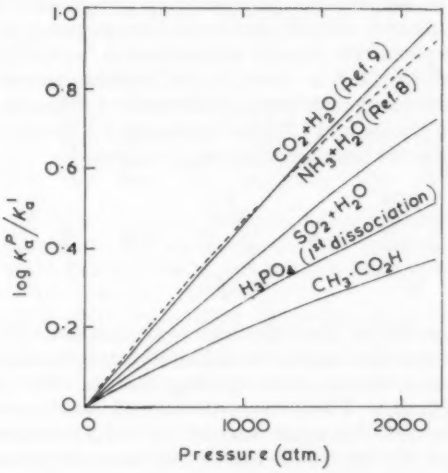
The differences between the ratios obtained for each salt at constant pressure and at various concentrations were within the limits of experimental error.

TABLE 4. *Effect of pressure on the ionization of acetic acid. Comparison of two sets of values of the acid dissociation constant* K_a ($\times 10^5$) *at high pressures and* 25°.

Author	K_a^1	K_a^{500}	K_a^{1000}	K_a^{2000}	ΔV^1	ΔV^{2000}	Average $10^3\Delta K$
This work	1·77	2·24	2·75	3·88	−12·1	−7·4	−2·4
Hamann [8]	1·71	—	2·70	3·91	−12·2	−7·3	−2·5

DISCUSSION

The Figure, which summarizes the results for the three acids as a graph of log (K_a^P/K_a^1) against pressure (superscripts refer to pressures), also includes published results for the ionization of ammonia [8] and carbon dioxide [9] at 25°. There is good agreement between the present results for acetic acid and those of Hamann.[8] A value of ΔV^1 equal to −16·2



c.c. mole^{-1}, obtained by density measurements,[11] for the first ionization constant of phosphoric acid is in reasonable agreement with our value (−15·5 c.c./mole).

The change with pressure of the ionization of sulphur dioxide solutions is less than for ammonia and carbon dioxide. It is, however, greater than the effects for the simple weak acids, acetic and phosphoric, as would be expected if sulphur dioxide is only slightly hydrated in solution.

As there is little reason for the partial molar volume of the bisulphite ion to be unusually high, the lower pressure effect for sulphur dioxide solutions relative to the other two hydrated gas systems must be due to a low partial molar volume for sulphur dioxide in solution. This is possibly owing to sulphur dioxide, with its high dipole moment and large radius, interacting with and tending to collapse the open structure of liquid water. Carbon dioxide by comparison is a smaller molecule with zero dipole moment. Ammonia, although having a high dipole moment, is of a similar size to the water molecules and probably has a smaller effect than sulphur dioxide on the water structure.

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[*Received, September 5th*, 1960.]

[11] Smith, Diss., 1943, Yale University.

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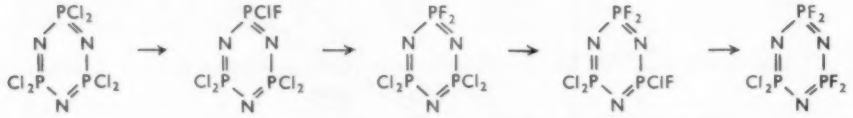
343. *Phosphonitrilic Derivatives. Part V.*[1] *The Triphosphonitrilic Fluoride Chlorides.*

By A. C. Chapman, D. H. Paine, H. T. Searle, D. R. Smith, and R. F. M. White.

Triphosphonitrilic trifluoride trichloride, $P_3N_3F_3Cl_3$, and new isomers of triphosphonitrilic difluoride tetrachloride, $P_3N_3F_2Cl_4$, and triphosphonitrilic tetrafluoride dichloride, $P_3N_3F_4Cl_2$, have been isolated from the products of partial fluorination of triphosphonitrilic chloride. The infrared and nuclear magnetic resonance spectra of these compounds and of the previously reported isomer of the tetrafluoride dichloride enable assignments of their structures to be made. These structures and the relative yields of the compounds show that a PFCl group is more easily fluorinated than a PCl_2 group.

The reaction of potassium fluorosulphite with the cyclic phosphonitrilic chlorides has previously been used to prepare the corresponding phosphonitrilic fluorides.[2,3] Some trimeric phosphonitrilic fluoride chlorides have now been prepared by allowing only partial reaction between triphosphonitrilic chloride and potassium fluorosulphite. The previously reported tetrafluoride dichloride[4] is shown to be triphosphonitrilic 1,1,3,3-tetrafluoride 5,5-dichloride, and the new compounds triphosphonitrilic 1,1-difluoride 3,3,5,5-tetrachloride, 1,1,3-trifluoride 3,5,5-trichloride, and 1,1,3,5-tetrafluoride 3,5-dichloride have been isolated. The following sequence for the main substitutions is suggested.



This sequence is supported by the high yields of the tetrafluoride dichloride relative to that of the trifluoride trichloride, and of the difluoride tetrachloride relative to that of the absent monofluoride pentachloride, both showing that a PFCl group is more easily fluorinated than a PCl_2 group. Further support comes from the absence of the 1,3,5-trifluoride 1,3,5-trichloride and the small amount of 1,1,3,5-tetrafluoride 3,5-dichloride formed, although some of this low-boiling isomer may have evaporated during storage.

The preferential fluorination of a PFCl group would be expected on the simple basis that the susceptibility of the phosphorus atom to nucleophilic attack should be increased by a single substituent of higher electronegativity than chlorine. It is interesting to contrast these results with those obtained in work on the replacement of the chlorine atoms by amine groups,[5] where successive replacement normally occurs at different phosphorus atoms. This may be partly due to steric hindrance, but in view of the known tendency of phosphorus and other second-row elements to accept electrons from neighbouring atoms,[6] it is probable that a second replacement at the same phosphorus atom in these cases is also hindered by the partial feed-back of " lone-pair " electrons from nitrogen atoms in the substituent groups.

Experimental

Materials.—Potassium fluorosulphite was prepared by shaking anhydrous potassium fluoride with liquid sulphur dioxide in an autoclave for 12—16 days. The increase in weight of the

[1] Part IV, Hartley, Paddock, and Searle, *J.*, 1961, 430.
[2] Seel and Langer, *Angew. Chem.*, 1956, **68**, 461.
[3] Part III, Chapman, Paddock, Paine, Searle, and Smith, *J.*, 1960, 3608.
[4] Schmitz-Dumont and Braschos, *Z. anorg. Chem.*, 1939, **243**, 113.
[5] Becke-Goehring and John, *Angew. Chem.*, 1957, **70**, 657; Ray and Shaw, *Chem. and Ind.*, 1959, 53; Becke-Goehring, John, and Fluck, *Z. anorg. Chem.*, 1959, **302**, 103.
[6] Henbest, *Ann. Reports*, 1956, **53**, 137.

solid indicated the composition $KF : SO_2 = 1 : 0{\cdot}5$—$0{\cdot}6$. Other materials have been described previously.[3]

Preparation of Phosphonitrilic Fluoride Chlorides.—In one experiment, an intimate mixture of potassium fluorosulphite and triphosphonitrilic chloride was heated at 120—140°. After removal of dissolved sulphur dioxide, the volatile products were distilled to yield a colourless liquid mixture of fluoride chlorides. In the second preparation, a mixture of triphosphonitrilic chloride and anhydrous potassium fluoride was heated with sulphur dioxide in a rocking autoclave at 110° for 7½ days. Volatile products were distilled off *in vacuo* and fractionated into triphosphonitrilic fluoride and a colourless liquid mixture of fluoride chlorides. This was combined with the product from the first experiment and again fractionated (reflux ratio greater than 30). The fractions were combined into five groups on the basis of their infrared spectra (CS_2 solution; Perkin–Elmer model 21 spectrometer).

Characterisation of Triphosphonitrilic Fluoride Chlorides.—The following fractions were identified: (1) 1,1,3,5-tetrafluoride 3,5-dichloride (0·5 g.), b. p. 84·4° ± 0·2°, ν (P=N) 1283, 1276; (2) 1,1,3,3-tetrafluoride 5,5-dichloride (21·6 g.), b. p. 114·7° ± 0·2° (lit.,[4] 115—117°), ν (P=N) 1277, 1253; (3) 1,1,3-trifluoride 3,5,5-trichloride (1·5 g.), b. p. 150·1° ± 0·2°, ν (P=N) 1258, 1237; and (4) 1,1-difluoride 3,3,5,5-tetrachloride (5·8 g.), b. p. 181·6° ± 0·2°, ν (P=N) 1246, 1226. Analyses are tabulated. Identifications are described below. Previous values [3,7] of ν (P=N) are 1297 cm.$^{-1}$ for $(PNF_2)_3$ and 1218 cm.$^{-1}$ for $(PNCl_2)_3$.

	Found (%, except *M*)						Reqd. (%, except *M*)				
Fraction	P	N	F	Cl	*M*	Formula	P	N	F	Cl	*M*
1	—	—	26·6	—	—	$P_3N_3Cl_3F_4$	—	—	27·0	—	—
2	32·9	14·7	26·1	24·5	290	$P_3N_3Cl_2F_4$	33·0	14·9	27·0	25·2	282
3	—	13·8	19·1	35·7	307	$P_3N_3Cl_3F_3$	—	14·1	19·1	35·7	298
4	29·3	13·0	11·9	43·8	314	$P_3N_3Cl_4F_2$	29·5	13·3	12·1	45·1	315

The frequencies of the P=N stretching vibration follow a smooth trend with increasing fluorine substitution, and confirm that all the fractions are trimeric; if they were tetrameric the P=N frequencies would be expected to fall between those of the tetrameric chloride [7] (1315 cm.$^{-1}$) and the tetrameric fluoride [3] (1428 cm.$^{-1}$).

Vapour-phase chromatography showed that the purity of the separated compounds was approximately 89%, 94%, 97%, and 97% respectively for the four fractions. This technique also showed the presence of another compound, besides triphosphonitrilic chloride, in the distillation residue, but this compound could not be isolated in characterisable quantities. Minute quantities of several other compounds were also present in the various fractions.

Nuclear magnetic resonance spectra of the three main fractions were obtained with a Varian V4300B high-resolution spectrometer, operating at 12 Mc./sec. for phosphorus and at 40 and 12 Mc./sec. for fluorine. Specimens were contained in sealed tubes of outside diameter either 12 or 5 mm. The spectra show a great deal of fine structure, which was not always fully resolved. The main features of the spectra, however, provide sufficient structural information. An analysis of the spectrum of triphosphonitrilic difluoride tetrachloride will be published separately.

Structures of the Triphosphonitrilic Fluoride Chlorides.—(a) *Triphosphonitrilic* 1,1,3,3-*tetrafluoride* 5,5-*dichloride and* 1,1,3,5-*tetrafluoride* 3,5-*dichloride.* On the basis of the data in the Table, fraction 2 may be identified with the previously reported triphosphonitrilic tetrafluoride dichloride; [4] fraction 1 is a new isomer, *triphosphonitrilic* 1,1,3,5-*tetrafluoride* 3,5-*dichloride.*

For triphosphonitrilic tetrafluoride dichloride there may be three isomers, 1,1,3,3-, *cis*-1,1,3,5-, and *trans*-1,1,3,5-. Since triphosphonitrilic chloride [7] and fluoride [8] have D_{3h} symmetry, these fluoride chloride isomers probably have C_{2v}, C_s, and C_2 symmetry respectively. The degeneracy of the P=N ring stretching vibration [3] would be resolved in all the isomers. Since the deviation from three-fold symmetry in the 1,1,3,3-isomer (C_{2v}) is roughly twice that in the others, the splitting of the degenerate vibration should be much larger in the 1,1,3,3-isomer than in the other two isomers, in which the splittings would be about equal. On this basis, therefore, the high-boiling isomer (fraction 2) of the tetrafluoride dichloride (splitting 24 cm.$^{-1}$) may be identified with the 1,1,3,3-isomer (C_{2v}), and the low-boiling isomer (fraction 1) (splitting 7 cm.$^{-1}$) with one of the 1,1,3,5-isomers (C_s or C_2).

[7] Daasch, *J. Amer. Chem. Soc.*, 1954, **76**, 3403.
[8] Chapman, unpublished work.

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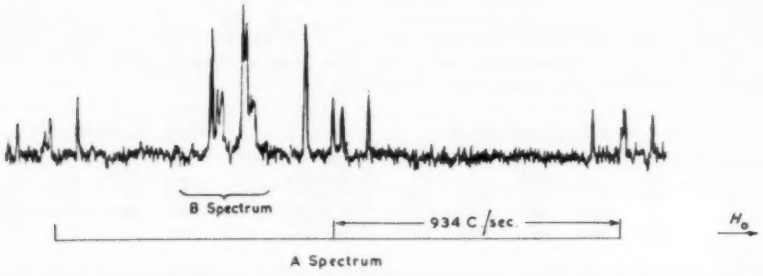
The fluorine nuclear magnetic resonance spectrum of fraction 2 consists of two peaks, each showing fine structure, with a separation of about 860 c./sec. at both 12 and 40 Mc./sec. This spectrum must be due to a single fluorine species, spin–spin coupled with phosphorus, showing that the compound must be the 1,1,3,3-tetrafluoride 5,5-dichloride. The phosphorus spectrum confirms this, being of the type [9] AB_2 with the B spectrum split into a triplet of separation 860 c./sec.

(b) *Triphosphonitrilic* 1,1-*difluoride* 3,3,5,5-*tetrachloride*. Fraction 4 may be identified as this compound, but the discrepancy between the present b. p. and that previously reported [4] suggests that the present compound is a different isomer. There are three possible isomers, having similar substitution types and symmetries to those of the tetrafluoride dichloride. Since fraction 4 has a splitting (20 $cm.^{-1}$) comparable with that of the 1,1,3,3-tetrafluoride 5,5-dichloride, this product may be identified with the 1,1-*difluoride* 3,3,5,5-*tetrachloride*.

Phosphorus nuclear magnetic resonance spectrum of triphosphonitrilic 1,1-*difluoride* 3,3,5,5,-*tetrachloride*.



The phosphorus nuclear magnetic resonance spectrum, shown in the Figure, is basically of the type AB_2, the phosphorus spin–spin coupling being comparable with the chemical shift between the two phosphorus species. The A spectrum is split into a triplet with a separation of 934 c./sec. This spectrum therefore confirms the 1,1-difluoride tetrachloride structure; the alternative 1,3-difluoride 1,3,5,5-tetrachloride structure would give a doublet splitting of the B spectrum of 934 c./sec. and no first-order A splitting.

The fluorine spectrum, both at 40 and at 12 Mc./sec., consists of two peaks separated by 934 c./sec. each showing fine structure. There is no indication of non-equivalence of fluorine atoms due to non-planarity of the ring.

The discrepancy between the b.p. of triphosphonitrilic 1,1-difluoride 3,3,5,5-tetrachloride and that previously reported for this compound [4] suggests that the earlier compound was not the 1,1-difluoride. This is most surprising, since the previously reported difluoride tetrachloride was obtained with the 1,1,3,3-tetrafluoride 5,5-dichloride from a high polymer of tetraphosphonitrilic tetrafluoride tetrachloride.[4] However, the suggestion is supported empirically by the fact that the b. p.s of triphosphonitrilic fluoride (51°), the 1,1,3,3-tetrafluoride 5,5-dichloride (114·7°), the 1,1,3-trifluoride 3,5,5-trichloride (150·1°), the 1,1-difluoride 3,3,5,5-tetrachloride (181·6°) and the chloride (256°) all lie on a smooth curve when plotted against the degree of substitution, while the value reported previously for the difluoride tetrachloride lies below the curve, in much the same way as the value for the 1,1,3,5-tetrafluoride 3,5-dichloride does.

(c) *Triphosphonitrilic* 1,1,3-*trifluoride* 3,5,5-*trichloride*. Fraction 3 may be identified as this *compound*. There are three possible isomers, 1,1,3-, *cis*-1,3,5-, and *trans*-1,3,5-, of probable symmetry C_1, C_{2v}, and C_s respectively. The splitting of the degenerate P=N vibration should be absent in the *cis*-1,3,5-isomer (C_{2v}), very small in the *trans*-1,3,5-isomer, and comparable with the splittings for the 1,1,3,3-tetrafluoride 5,5-dichloride and the 1,1-difluoride 3,3,5,5-tetrachloride in the 1,1,3-trifluoride. In fact the splitting (21 $cm.^{-1}$) is very similar to those for the 1,1,3,3-tetrafluoride 5,5-dichloride and the 1,1-difluoride 3,3,5,5-tetrachloride, and the trichloride may therefore be identified with the 1,1,3-isomer (C_1). This structure is also consistent with the formation of the trifluoride trichloride by fluorination of the 1,1-difluoride tetrachloride.

[4] Pople, Schneider, and Bernstein, " High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959, p. 123.

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The fluorine spectrum consists of two doublets, of relative areas ~2 : 1, having field independent separations of 880 and 1000 c./sec., respectively, for the stronger and the weaker doublet. The separation between the centres of the two doublets is 460 c./sec. at 12 Mc./sec. and 1600 c./sec. at 40 Mc./sec. The molecule therefore contains two fluorine species in relative amounts 2 : 1, each fluorine atom being spin–spin coupled to a phosphorus atom. This spectrum is therefore consistent with either the 1,1,3- or the *trans*-1,3,5-trifluoride.

The phosphorus spectrum of the *trans*-1,3,5-isomer would be of type AB_2, with both the A and B spectra split into doublets by phosphorus–fluorine coupling. Since the phosphorus atoms would be chemically equivalent, the chemical shift between the phosphorus species, arising only from the non-equivalence of the fluorine atoms, would be very small; the spectrum would therefore consist of two groups of lines separated by about 1000 c./sec. The phosphorus spectrum of the 1,1,3-isomer, on the other hand, would be of type ABC, with the A spectrum split into a triplet and the B into a doublet by spin–spin interaction with the fluorine nuclei. The spectrum would contain many lines spread over a range of about 2000 c./sec. The observed phosphorus spectrum is in agreement with this, extending over nearly 2000 c./sec., with a singlet/doublet/triplet structure just discernible, confirming that the compound is the 1,1,3-isomer.

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344. *Studies of Trifluoroacetic Acid. Part XVIII.*[1] *Reaction of N-Aroylglycines with Perfluoro-carboxylic Anhydrides.*

By E. J. BOURNE, J. BURDON, V. C. R. MCLOUGHLIN, and J. C. TATLOW.

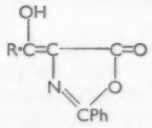
Trifluoroacetic anhydride with hippuric acid gave 2-phenyl-4-(2,2,2-trifluoro-1-hydroxyethylidene)oxazol-5-one (II) in 90% yield. With water this gave 1-benzamido-3,3,3-trifluoropropane-2,2-diol (VI). Pentafluoropropionic and heptafluorobutyric anhydrides afforded analogous products. *N*-Anisoyl- and *N*-*p*-nitrobenzoyl-glycine also gave oxazolones with trifluoroacetic anhydride. The ketone hydrate (VI) has been reduced to the alcohol: it also formed a cyanohydrin (XI) which was hydrolysed to β-amino-α-hydroxy-α-trifluoromethylpropionic acid (XII).

ATTENBURROW, ELLIOTT, and PENNY [2] treated sodium hippurate with acetic anhydride in the presence of a heterocyclic base and obtained 4-1′-hydroxyethylidene-2-phenyloxazol-5-one (I), and this reaction was extended by Bullerwell and Lawson [3] to other anhydrides, compounds corresponding to (I) being produced. We have found that hippuric acid and trifluoroacetic anhydride react in a similar way, to give the pale yellow oxazolone (II). Other carboxylic acid–trifluoroacetic anhydride mixtures form [4] powerful acylating reagents; this cyclisation could proceed through such an intermediate. Compound (II) was best obtained (90% yield) by using a three-fold excess of trifluoroacetic anhydride in acetone.

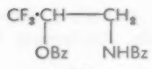
The oxazolone structure (II), based on analogy [2,3] and analyses, is confirmed by other results. The compound gave a green colour with ferric chloride (enol) and was sufficiently acidic to be titrated with phenolphthalein as indicator. The ultraviolet spectrum was similar to those [5] for 4-alkylidene-2-aryloxazol-5-ones with a hetero-atom at position 1′:

[1] Part XVII, Bourne, Burdon, and Tatlow, *J.*, 1959, 1864.
[2] Attenburrow, Elliott, and Penny, *J.*, 1948, 310.
[3] Bullerwell and Lawson, *J.*, 1952, 1350.
[4] Tedder, *Chem. Rev.*, 1955, **55**, 787; Bourne, Stacey, Tatlow, and Worrall, *J.*, 1958, 3268.
[5] Sheinker and Golovner, *Doklady Akad. Nauk S.S.S.R.*, 1951, **79**, 269 (*Chem. Abs.*, 1952, **46**, 35i); Trenner in "The Chemistry of Penicillin," ed. Clarke, Johnson, and Robinson, Princeton Univ. Press, Princeton, N.J., 1949, p. 429.

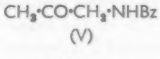
such compounds usually show a band between 230 and 300 mμ (ε *ca.* 10,000) and a stronger one between 320 and 400 mμ (ε *ca.* 25,000). Compound (II) had an inflexion at 300 mμ (ε 9700) and a maximum at 345 mμ (ε 23,800). Further, reaction with boiling water gave carbon



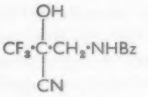
(I) R = CH_3
(II) R = CF_3
(III) R = C_2F_5
(IV) R = C_3F_7



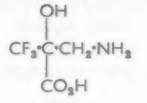
(IX)



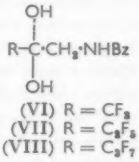
(V)



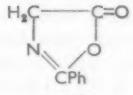
(XI)



(XII)



(VI) R = CF_3
(VII) R = C_2F_5
(VIII) R = C_3F_7



(X)

dioxide and 1-benzamido-3,3,3-trifluoropropane-2,2-diol (VI) (84% yield), and the latter was reduced with Raney nickel and hydrogen or sodium borohydride to the benzamido-alcohol [isolated as the known [6] *O*-benzoyl derivative (IX)]. The reaction with water presumably occurred by hydrolysis, ketonisation, and decarboxylation of the resultant β-keto-acid. The process is similar to the conversions of the oxazol-5-one [2] (I) and its homologues [3] into carbon dioxide and alkyl benzamidomethyl ketones (*e.g.*, V) by boiling water, and to the Dakin–West reaction [7] in which *N*-acylamino-acids are converted by acetic anhydride in pyridine into *N*-acylaminoalkyl methyl ketones [the Dakin–West reaction is supposed [2] to involve hydrolysis and subsequent decarboxylation of oxazolones analogous to (I)].

The ketone hydrate (VI) formed a cyanohydrin (XI) in 58% yield on being treated with potassium cyanide and then sulphuric acid. This cyanohydrin was hydrolysed by acid to give, in low yield, the known [8] β-amino-α-hydroxy-α-trifluoromethylpropionic acid (XII). In an attempted hydrolysis of the ketone hydrate (VI) to the unknown 1-amino-3,3,3-trifluoropropan-2-one, only benzoic acid was isolated.

Reactions of hippuric acid with pentafluoropropionic and heptafluorobutyric anhydride similarly gave high yields of the coloured oxazolones (III and IV) which had ultraviolet spectra very similar to that of the oxazolone (II). These compounds, in boiling water, gave the corresponding α-benzamido-ketone hydrates (VII and VIII in good yields. Also, *N*-*p*-anisoyl- and *N*-*p*-nitrobenzoyl-glycine with trifluoroacetic anhydride gave the analogous 2-*p*-methoxyphenyl- and 2-*p*-nitrophenyl-4-(2,2,2-trifluoro-1-hydroxyethylidene)oxazol-5-ones, the last in 60% yield even without acetone as diluent. The *p*-nitrophenyloxazolone was hydrolysed to the corresponding 1-*p*-nitrobenzamido-ketone.

N-Cinnamoyl-, *N*-furoyl-, *N*-*o*-nitrobenzoyl-, and *N*-(3,5-dinitrobenzoyl)-glycine all reacted with trifluoroacetic anhydride to give coloured products, which were probably analogous oxazolones but could not be purified sufficiently to give correct analyses.

The formation of the oxazolones (II, III, and IV) probably proceeded *via* 2-phenyloxazol-5-one (X) itself formed by dehydration of hippuric acid by the anhydride, since this oxazolone (X) reacted with one molecular proportion of trifluoroacetic anhydride to give the product (II) in 81% yield. Attenburrow *et al.*[2] also considered 2-phenyloxazol-5-one (X) to be an intermediate; acetic anhydride [3] with hippuric acid gave the oxazolone (X), but, in the absence of a basic catalyst, further reaction to give the 4-substituted oxazolone

[6] Jones, *J. Amer. Chem. Soc.*, 1948, **70**, 143.
[7] Dakin and West, *J. Biol. Chem.*, 1928, **78**, 91, 745.
[8] Burdon, McLoughlin, and Tatlow, *J.*, 1960, 3184.

XUM

(I) did not occur.[2] That perfluoro-carboxylic anhydrides react with the oxazolone (X) in the absence of a base is probably due to the greater electrophilic character of the carbon atoms of their carbonyl groups. The reaction between aromatic aldehydes and the oxazolone (X) also takes place [9] in the absence of a base: the carbonyl group of an aromatic aldehyde would be expected to be more electrophilic than that of an alkanecarboxylic anhydride. It is also possible that the perfluorocarboxylic acids formed during the reactions might, as they are strong acids, increase the electrophilic nature of the anhydride carbonyl groups by protonation.[10] Thus, perfluoro-carboxylic anhydrides should react with other activated methylene groups in the absence of basic catalysts; preliminary work shows this to be so.

An attempt has been made to extend the reaction to *N*-aroyl derivatives of amino-acids other than glycine. However, under the conditions described in this paper, we have found no analogous oxazolones among the products; this could, as a Referee suggested, be because stabilisation by enolisation (cf. I—IV) cannot take place.

Experimental

Treatment of Hippuric Acid with Perfluoro-carboxylic Anhydrides.—(a) *Trifluoroacetic anhydride.* The anhydride (5·8 ml.) was added to a suspension of hippuric acid (2·50 g.) in dry acetone (20 ml.). The mixture became warm and the hippuric acid dissolved in about 15 min. to give a red solution. After 17 hr. at 10—15° a deep red precipitate had been formed and the mixture was poured into water (400 ml.). The pink precipitate was filtered off and washed with water to give material (3·23 g.), m. p. 225—229° (decomp.), which was sufficiently pure for most purposes. A sample (0·25 g.), recrystallised from benzene (*ca.* 100 ml.), gave the very pale yellow *2-phenyl-4-(2,2,2-trifluoro-1-hydroxyethylidene)oxazol-5-one* (II) (0·12 g.), m. p. 227—231° (decomp; depending on the rate of heating) (Found: C, 51·1; H, 2·3%; equiv., 254. $C_{11}H_6F_3NO_3$ requires C, 51·4; H, 2·4%; equiv., 257). The equivalent weight was determined potentiometrically against 0·05N-sodium hydroxide in 0·01M-solution, the end-point being at about pH 7·5. The compound had $\lambda_{max.}$ at 345 mμ (ε 23,800) and a broad inflexion at 300 mμ (ε 9700) in ethanol: it gave a deep green colour with ethanolic ferric chloride.

A reaction carried out in the absence of acetone gave only a 50% yield of the oxazolone and much tar.

(b) *Pentafluoropropionic anhydride.* Hippuric acid (1·70 g.) was treated with pentafluoropropionic anhydride (8·80 g.) in dry acetone (15 ml.), as in (a), to give an orange-yellow crude product (2·09 g.), m. p. *ca.* 200—205° (decomp.), which was recrystallised from benzene to give yellow *4-(2,2,3,3,3-pentafluoro-1-hydroxypropylidene)-2-phenyloxazol-5-one* (III) (1·45 g.), m. p. *ca.* 210—215° (decomp.); this m. p. varied greatly with the rate of heating, the one quoted was obtained by placing the sample in a heated (*ca.* 150°) zone and then raising the temp. to the m. p. in 1—2 min. The compound will melt with decomposition at 160° if kept at this temperature for about 30 min. (Found: C, 47·1; H, 1·8. $C_{12}H_6F_5NO_3$ requires C, 46·9; H, 2·0%). In ethanol the compound had $\lambda_{max.}$ at 346 mμ (ε 19,400) and a broad inflexion at 301 mμ (ε 8000).

(c) *Heptafluorobutyric anhydride.* Hippuric acid (2·00 g.) was treated with heptafluorobutyric anhydride (13·7 g.) in dry acetone (15 ml.), as in (a). The crude product was taken up in 0·5N-sodium hydroxide (200 ml.), and the resulting solution was filtered and acidified with 4N-sulphuric acid (this removed most of the absorbed heptafluorobutyric acid). The precipitated yellow solid (3·30 g.), m. p. 220—223° (decomp.), was recrystallised from benzene, to give the pale yellow-green *4-(2,2,3,3,4,4,4-heptafluoro-1-hydroxybutylidene)-2-phenyloxazol-5-one* (IV) (2·73 g.), m. p. 226—228° (decomp.) (Found: C, 43·6; H, 1·8. $C_{13}H_6F_7NO_3$ requires C, 43·7; H, 1·7%). In ethanol the compound had $\lambda_{max.}$ at 347 mμ (ε 23,100) and a broad inflexion at 300 mμ (ε 8800).

In the absence of acetone only a 21% yield was obtained.

Reaction of 2-Phenyloxazol-5-one (X) *with Trifluoroacetic Anhydride.*—Trifluoroacetic

[9] Crawford and Little, *J.*, 1959, 729.
[10] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, p. 676.

anhydride (0·43 ml.) was added to a solution of 2-phenyloxazol-5-one (0·50 g.) in dry acetone (5 ml.). Treatment as in (a) above gave 2-phenyl-4-(2,2,2-trifluoro-1-hydroxyethylidene)-oxazol-5-one (II) (0·65 g.), m. p. and mixed m. p. 224—228° (decomp.).

Reaction of N-p-*Anisoylglycine with Trifluoroacetic Anhydride.*—*N-p*-Anisoylglycine (0·50 g.), suspended in dry acetone (2·5 ml.), was treated with trifluoroacetic anhydride (1·1 ml.) as in (a) above. The brown solid (0·69 g.), m. p. 175—185° (decomp.), was twice precipitated from acetone solution with light petroleum (b. p. 80—100°), to give the pale brown 2-p-*methoxyphenyl*-4-(2,2,2-*trifluoro*-1-*hydroxyethylidene*)*oxazol*-5-*one* (0·23 g.), m. p. 225—228° (decomp.; depending on the rate of heating) (Found: C, 50·4; H, 3·2. $C_{12}H_8F_3NO_4$ requires C, 50·2; H, 2·8%).

Reaction of N-p-*Nitrobenzoylglycine with Trifluoroacetic Anhydride.*—Trifluoroacetic anhydride (2·3 ml.) and *N-p*-nitrobenzoylglycine (0·75 g.) were refluxed together for 30 min. (there was no reaction at room temperature) and the resulting orange solution was kept at 10—15° for 24 hr. The red crystals which had been formed were filtered off, washed with carbon tetrachloride, and recrystallised from ethanol–carbon tetrachloride to give 2-p-*nitrophenyl*-4-(2,2,2-*trifluoro*-1-*hydroxyethylidene*)*oxazol*-5-*one* (0·61 g.), m. p. 212—214° (decomp.) (Found: C, 43·4; H, 1·6. $C_{11}H_5F_3N_2O_6$ requires C, 43·7; H, 1·7%).

Hydrolysis of the Oxazolones.—(a) 2-*Phenyl*-4-(2,2,2-*trifluoro*-1-*hydroxyethylidene*)*oxazol*-5-*one* (II). This compound (14·3 g.) was refluxed with water (50 ml.) for 1 hr., slowly dissolving while carbon dioxide was evolved (lime-water test). The colourless solution was extracted continuously with ether for 14 hr., and the extracts were dried ($MgSO_4$) and evaporated, to leave 1-*benzamido*-3,3,3-*trifluoropropane*-2,2-*diol* (VI) (11·65 g.), m. p. 107—109° (from benzene) (Found: C, 48·3; H, 3·9. $C_{10}H_8F_3NO_2,H_2O$ requires C, 48·2; H, 4·0%). In ethanol–hydrochloric acid this gave its 2,4-*dinitrophenylhydrazone*, m. p. 194—195° (from aqueous ethanol), depressed on admixture with 2,4-dinitrophenylhydrazine (Found: C, 46·8; H, 2·8. $C_{16}H_{13}F_3N_6O_5$ requires C, 46·7; H, 2·9%).

Hydrolysis of the ketone hydrate (VI) for 4 hr. with 5N-hydrochloric acid under reflux gave a quantitative yield of benzoic acid, but no other product could be isolated.

(b) 2-p-*Nitrophenyl*-4-(2,2,2-*trifluoro*-1-*hydroxyethylidene*)*oxazol*-5-*one*. This compound (0·25 g.) was refluxed with water (5 ml.). Isolation as in (a) gave 1,1,1-*trifluoro*-3-p-*nitrobenzamidopropane*-2,2-*diol* (0·05 g.), m. p. 106—107° (from benzene) (Found: C, 40·4; H, 2·8. $C_{10}H_7F_3N_2O_4,H_2O$ requires C, 40·8; H, 3·1%).

(c) 4-(2,2,3,3,3-*Pentafluoro*-1-*hydroxypropylidene*)-2-*phenyloxazol*-5-*one* (III). This compound (0·70 g.) was refluxed with water (100 ml.) for 1 hr. The colourless solution was filtered while hot to remove tar and then cooled to 0°. The crystals formed were 1-*benzamido*-3,3,4,4,4-*pentafluorobutane*-2,2-*diol* (VII) (0·33 g.), m. p. 96—98° (unchanged on recrystallisation from water) (Found: C, 44·1; H, 3·7. $C_{11}H_8F_5NO_2,H_2O$ requires C, 44·2; H, 3·4%).

(d) 4-(2,2,3,3,4,4,4-*Heptafluoro*-1-*hydroxybutylidene*)-2-*phenyloxazol*-5-*one* (IV). This compound (0·95 g.) was refluxed with water (400 ml.) as in (c), to give 1-*benzamido*-3,3,4,4,5,5,5-*heptafluoropentane*-2,2-*diol* (VIII) (0·61 g.), m. p. 86—88° (Found: C, 41·1; H, 2·8. $C_{12}H_8F_7NO_2,H_2O$ requires C, 41·3; H, 2·9%).

N-(2-*Benzoyloxy*-3,3,3-*trifluoropropyl*)*benzamide* (IX).—(*a*) A solution of the ketone hydrate (VI) (0·50 g.) in ethanol (50 ml.) containing Raney nickel (*ca.* 1 g.) was hydrogenated at room temperature and atmospheric pressure for 23 hr. About 42 ml. of hydrogen were taken up. The solution was filtered, the ethanol evaporated, and the solid residue treated with benzoyl chloride (1 ml.) in pyridine (20 ml.) at 10—15° for 13 hr. The mixture was poured into water and recrystallisation of the precipitate from aqueous ethanol afforded the *ON*-dibenzoyl derivative (IX) (0·43 g.), m. p. 127—128° (lit.,[6] 126·5—127·5°) (Found: C, 60·2; H, 4·1. Calc. for $C_{17}H_{14}F_3NO_3$: C, 60·5; H, 4·2%).

(*b*) A solution of sodium borohydride (0·30 g.) in water (5 ml.) was added to a solution of the ketone hydrate (0·10 g.) in water (10 ml.). Vigorous evolution of gas took place. After 3 hr. at 10—15°, 11N-hydrochloric acid (0·25 ml.) was added to destroy the excess of borohydride, followed by 10N-sodium hydroxide (5 ml.). Treatment with benzoyl chloride gave a precipitate of the dibenzoyl derivative (0·13 g.), m. p. and mixed m. p. 127—128°, unchanged by recrystallisation from aqueous ethanol.

β-*Benzamido*-α-*hydroxy*-α-*trifluoromethylpropionitrile* (XI).—1-Benzamido-3,3,3-trifluoropropane-2,2-diol (VI) (1·0 g.) was added to a solution of potassium cyanide (0·35 g.) in water (25 ml.) cooled to 0°. The ketone dissolved during 1 hr. as the mixture was stirred. Addition

of 3N-sulphuric acid then precipitated the crude cyanohydrin, which was filtered off, and the aqueous phase was extracted with ether. Recrystallisation from benzene gave β-*benzamido-α-hydroxy-α-trifluoromethylpropionitrile* (XI) (0·6 g.), m. p. 111—113°, depressed on admixture with the starting material (Found: C, 51·0; H, 3·6; F, 22·3. $C_{11}H_9F_3N_2O_2$ requires C, 51·2; H, 3·5; F, 22·1%).

β-*Amino-α-hydroxy-α-trifluoromethylpropionic Acid* (XII).—The cyanohydrin (XI) (2·70 g.) was added, with stirring, to 98% sulphuric acid (3·5 ml.) and the solution was heated at 110° for 1 hr. Water (3 ml.) was added to the cooled mixture, and the resulting solution was refluxed for 2 hr. On being cooled, the solution deposited benzoic acid (1·28 g.), m. p. and mixed m. p. 119—120°, which was filtered off. The filtrate was neutralised with barium carbonate, the insoluble barium salts were filtered off and washed with warm water, and the combined filtrate and washings were evaporated to dryness *in vacuo*. The solid residue (0·23 g.) recrystallised from aqueous ethanol, to give β-amino-α-hydroxy-α-trifluoromethylpropionic acid (XII) (0·22 g.), m. p. 310° (decomp.). This compound had an infrared spectrum identical with that of material reported [8] previously.

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345. *Chemical and Magnetic Properties of Lanthanum Dicarbide and Sesquicarbide.*

By N. N. GREENWOOD and A. J. OSBORN.

Lanthanum dicarbide and sesquicarbide have been prepared by heating lanthanum dihydride with the stoicheiometric amounts of graphite. The dicarbide is diamagnetic and the sesquicarbide very slightly paramagnetic, indicating almost complete delocalization of the extra valency electrons in a conduction band. Reactions of the carbides with a variety of reagents have been studied and compared with the corresponding reactions of calcium carbide, the gaseous products being identified and quantitatively determined by infrared spectroscopy and gas–liquid chromatography.

LANTHANUM DICARBIDE is isostructural with calcium carbide [1] and has been formulated as an ionic acetylide. As lanthanum ($5d^16s^2$) is normally tervalent, interest in the compound centres on the position of the third valency electron and on the influence of this electron on the chemistry of the compound. Three possibilities have been considered for the ground-state configuration of the compound: (*a*) the electron is localized on the lanthanum ion, giving rise to a bivalent acetylide $La^{2+}C_2^{2-}$; (*b*) the electron is localized in an antibonding orbital of the acetylide ion, giving $La^{3+}C_2^{3-}$; (*c*) the electron, e, is delocalized in a conduction band of the crystal, $La^{3+}C_2^{2-} + e$. Model (*a*) would explain the similarity in structure to calcium carbide, $Ca^{2+}C_2^{2-}$, and the fact that a variety of hydrocarbons rather than pure acetylene is evolved on hydrolysis.[2] Model (*b*) would explain the C–C distance, which is intermediate between those characteristic of a double and a triple bond.[3] However, both are inconsistent with the observed metallic conductivity of the dicarbide which approaches that of lanthanum itself.[4] It is clear that model (*c*) is an important component of the electronic state of the crystal, but the conductivity, by itself, does not rule out some admixture of the states (*a*) and (*b*). The crucial test is the

[1] Von Stackelberg, *Z. phys. Chem.*, 1930, *B*, **9**, 437.
[2] Wells, "Structural Inorganic Chemistry," Oxford University Press, 2nd edn., 1950.
[3] Atoji, Gschneidner, Daane, Rundle, and Spedding, *J. Amer. Chem. Soc.*, 1958, **80**, 1804.
[4] Spedding, Gschneidner, and Daane, *Trans. Met. Soc., A.I.M.E.*, 1959, **215**, 192; *J. Amer. Chem. Soc.*, 1958, **80**, 4499.

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magnetic susceptibility since (*a*) and (*b*), which involve localized unpaired electrons, must confer some paramagnetism on the crystal whereas model (*c*) is essentially diamagnetic.

Lanthanum sesquicarbide, La_2C_3, also contains C_2 units in its structure [3] and has a conductivity approximately two-fifths that of metallic lanthanum.[4] Similar possibilities can be envisaged for its electronic structure and again it is clear that any tendency towards localization of electrons on either the lanthanum or the acetylide ion would lead to paramagnetism. The magnetic measurements reported in this paper were undertaken to determine whether such localization occurs.

Lanthanum dicarbide was first prepared [5] by heating lanthanum sesquioxide with carbon in an electric furnace, and most subsequent investigators have used this procedure or modifications of it,[1,6-9] although the product is invariably contaminated with oxide or carbon. The dicarbide has also been prepared by direct reaction of metallic lanthanum and carbon in an arc furnace under helium or argon.[4] The sesquicarbide has only recently been reported; [3] it was made from the elements at temperatures below its incongruent m. p., 1415°. The hydride method used in the present work, though a standard procedure for preparing carbides, has not previously been used for the carbides of lanthanum.

The chemistry of the two carbides has previously been little studied. The products of hydrolysis by water or dilute acid have been investigated, with varying results, by conventional gas analysis and by mass spectroscopy (see Discussion). In addition, reactions of the dicarbide with several non-metallic elements and their derivatives have been studied at high temperatures, though the products were not always identified.[6,10]

We have used infrared spectroscopy and gas–liquid chromatography to analyse the products of hydrolysis of calcium carbide and the carbides of lanthanum by 4N-sulphuric acid and 2N-nitric acid. Other protonic reagents studied were anhydrous sulphuric acid, chlorosulphonic acid, and liquid ammonia. The reaction of the three carbides with molten iodine was also investigated.

Results

Lanthanum dicarbide formed greyish-yellow metallic-looking crystals, and *X*-ray powder photographs showed the symmetry to be body-centred tetragonal. Lattice constants were $a_0 = 3{\cdot}935 \pm 0{\cdot}005$, $c_0 = 6{\cdot}750 \pm 0{\cdot}005$ Å, in good agreement with the most accurate published data.[3] Lanthanum sesquicarbide formed brassy-yellow crystals which were indexed as body-centred cubic with $a_0 = 8{\cdot}810 \pm 0{\cdot}005$ Å (lit.,[3] $8{\cdot}817 \pm 0{\cdot}003$ Å). When heated above its incongruent m. p., the sesquicarbide disproportionated and, in an experiment at 2200°, metallic lanthanum volatilized continuously from the specimen leaving, eventually, the pure dicarbide: $2La_2C_3 = La + 3LaC_2$.

The magnetic susceptibilities (in units of 10^{-6} e.m.u. per mole) as measured by the Gouy method at room temperature were: $LaC_2 - 7{\cdot}17$, $LaC_{1{\cdot}5} + 25{\cdot}1$, $LaH_{2{\cdot}16} + 49{\cdot}4$. These can be compared with published values for the paramagnetic susceptibility of metallic lanthanum, *viz.*, +96 [11] and +101.[12] Absence of ferromagnetic impurities was confirmed by variation of the magnetic field.

The reaction of lanthanum dicarbide with deaerated 4N-sulphuric acid at room temperature was vigorous and exothermic. The gases evolved consisted mainly of acetylene, hydrogen, and ethylene, together with traces of carbon dioxide and methane as shown in Table 1. The higher hydrocarbon fraction contained virtually no C_3 compounds and was mainly C_4 hydrocarbons (Table 2). In addition to the gaseous products, which contained 1·46 g.-atoms of carbon per mole of LaC_2, a further 0·56 g.-atom of carbon was precipitated as the element,

[5] Pettersson, *Ber.*, 1895, **28**, 2419.
[6] Moissan, "The Electric Furnace," Chem. Publ. Co., Easton, Pa., 2nd edn., 1920.
[7] Damiens, *Compt. rend.*, 1913, **157**, 214; *Ann. Chim.* (*France*), 1918, **10**, 137.
[8] Villelume, *Compt. rend.*, 1950, **231**, 1497; 1951, **232**, 235.
[9] Vickery, Sedlacek, and Ruben, *J.*, 1959, 498.
[10] Delépine, Thèse Pharmacie, Paris, 1904, as quoted by Pascal, "Nouveau Traité de Chimie Minérale," Vol. VII, p. 857, Masson et Cie, Paris, 1959.
[11] Stalinski, *Bull. Acad. polon. Sci., Classe III*, 1957, **5**, 997.
[12] Lock, *Proc. Phys. Soc.*, 1957, **70**, *B*, 566.

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making 2·02 g.-atoms in all. The material balance on carbon (involving 150 mg. in a typical experiment) was therefore correct to 1%; this confirmed the infrared and chromatographic methods used to analyse the complex mixture of products, and also indicated the degree of absolute accuracy obtained.

Lanthanum sesquicarbide reacted even more vigorously with 4N-sulphuric acid and more carbon was precipitated (1·14 g.-atoms per mole of La_2C_3). Table 1 shows that the gases

TABLE 1. *Gaseous products of hydrolysis (volume %).*

System	H_2	CH_4	C_2H_2	C_2H_4	Higher hydrocarbons	CO	CO_2	N_2O	NO
LaC_2–H_2SO_4	17·9	0·2	68·3	8·9	4·2	—	0·4	—	—
La_2C_3–H_2SO_4	47·1	2·0	36·6	5·6	1·3	5·6	1·8	—	—
LaC_2–HNO_3	3·4	—	59·0	3·1	1·7	—	0·5	19·2	13·2
La_2C_3–HNO_3	16·4	1·4	50·3	3·8	7·6	—	0·3	16·9	3·6

TABLE 2. *Composition of the higher hydrocarbon fractions (volume %).*

System	C_3	Butane	But-1-ene	But-2-ene *cis*	But-2-ene *trans*	Buta-1,2-diene	Buta-1,3-diene	But-1-yne
LaC_2–H_2SO_4 ...	3·0	7·9	1·3	13·1	9·8	4·6	55·8	4·6
LaC_2–HNO_3 ...	2·6	2·6	8·0	5·5	8·0	2·6	70·8	—
La_2C_3–HNO_3 ...	26·6	4·4	3·4	6·2	4·4	1·3	49·4	4·2

evolved contained proportionately more hydrogen and less acetylene than the hydrolysis products from the dicarbide and there was also an appreciable amount of carbon monoxide, The higher hydrocarbons, which comprised 1·3% of the gases evolved, contained propane. propene, butane, but-1-ene, *cis*- and *trans*-but-2-ene, and traces of two other hydrocarbons. In all, the gaseous products contained 1·95 g.-atoms of carbon per mole of La_2C_3, making a total of 3·09 g.-atoms. In a control experiment, technical grade calcium carbide (containing calcium oxide as impurity) was hydrolysed with 4N-sulphuric acid under the same conditions; the reaction was much less vigorous and acetylene was evolved quantitatively. There was no other hydrocarbon, no oxides of carbon, and no hydrogen, nor was free carbon precipitated.

The products of hydrolysis of the lanthanum carbides are not independent of the aqueous acid used. For example, Table 1 indicates that hydrolysis of the dicarbide with 2N-nitric acid results in the evolution of considerable amounts of nitrous oxide and nitric oxide, and that this is accompanied by a reduction in the amount of hydrogen and ethylene evolved. The effect is only slightly less marked with the sesquicarbide; but, with calcium carbide, only acetylene and carbon dioxide (0·3% by volume) were evolved and there was no trace of oxides of nitrogen or of free carbon. The composition of the higher hydrocarbon fractions is summarized in Table 2. Butadiene is again seen to be the main constituent and, in the case of the sesquicarbide, the C_3 fraction is prominent, forming 26·6% of the higher hydrocarbons and therefore 2% of all the gaseous products of hydrolysis (cf. 0·04% of C_2 obtained on hydrolysis of the dicarbide with nitric acid). Less free carbon was precipitated in the nitric acid hydrolyses than in the sulphuric acid hydrolyses; the dicarbide gave 0·41 g.-atom of carbon per mole of LaC_2 and the sesquicarbide 0·73 g.-atom per mole of La_2C_3.

Anhydrous sulphuric acid reacted differently from the aqueous acid. At room temperature, calcium carbide gave a gas consisting of acetylene (98%) together with traces of carbon dioxide and sulphur dioxide. The amount of acetylene evolved corresponded to 89% of the carbon in the carbide, the rest being precipitated as free carbon. Reaction with lanthanum dicarbide was much slower and, after 30 min., only 5% of the C_2 units had reacted to give acetylene. A small amount of hydrogen was also evolved but no other gases were detected. The reaction appeared to be retarded by the formation of an insoluble film of lanthanum sulphate on the carbide. Control experiments indicated that the sulphate was moderately soluble in hot anhydrous sulphuric acid and could, in fact, be recrystallized from this solvent. Accordingly a reaction was run at 100°; gas was evolved over a period of 5 hr. after which time 35% of the carbide remained unchanged. The gas proved to be pure sulphur dioxide, all the carbon that reacted appearing as the free element or tar. Lanthanum sesquicarbide reacted rather more vigorously. The initial gases evolved were acetylene and hydrogen together with a trace of sulphur dioxide, but when the reaction had proceeded for 3 days (after which time 25% of the

carbide remained unchanged) only hydrogen and sulphur dioxide were detected. Small amounts of water in the sulphuric acid had no apparent effect on any of these reactions, the products from 99·8% and 96% sulphuric acid being the same as those from the 100% acid.

It was shown in separate series of experiments that acetylene reacted slowly with anhydrous sulphuric acid at room temperature to give sulphur dioxide as the only gaseous product; the reaction was faster at 100°, being complete in about 15 hr. This suggests that the sulphur dioxide appearing in the above reactions arose from the reduction of sulphuric acid by acetylene rather than from the direct reaction of sulphuric acid with the carbide, *e.g.*, $2LaC_2 + 6H_2SO_4 = La_2(SO_4)_3,6H_2O + 4C + 3SO_2$. The actual composition of the gases evolved depended on the temperature, and on the rate of removal of the products under vacuum from the reaction region. The absence of ethylene, even in the cold, does not necessarily imply that this gas was not formed initially since it is rapidly absorbed by anhydrous sulphuric acid and would not be expected to be evolved.

Chlorosulphonic acid reacted extremely vigorously with technical grade calcium carbide, but only slowly and incompletely with the carbides of lanthanum. With calcium carbide the main volatile product (87%) was hydrogen chloride, but acetylene, carbon monoxide, carbon dioxide, carbon oxysulphide, and sulphur dioxide were also produced in amounts which depended on the reaction temperature. Thus, when the reaction rate was moderated by intermittent cooling at −78°, the amount of acetylene evolved was more than doubled, but only two-thirds of the amount of carbon dioxide and sulphur dioxide, one-seventh of the amount of carbon oxysulphide and no carbon monoxide were formed. It was clear that acetylene was undergoing a secondary reaction with the chlorosulphonic acid and it was established that pure acetylene, when treated with chlorosulphonic acid at 100°, rapidly charred and evolved a mixture of the above gases. The formation of carbon oxysulphide is noteworthy.

By contrast, there was little reaction between chlorosulphonic acid and lanthanum dicarbide, and the presence of lanthanum oxide failed to accelerate the reaction. At 100° hydrogen chloride, sulphur dioxide, and small amounts of carbon dioxide and carbon oxysulphide were formed but no acetylene was evolved. When the excess of chlorosulphonic acid was removed and fractionated, more hydrogen chloride and sulphur dioxide were obtained, and also a trace of acetylene, equivalent to 0·5% of the C_2 units in the carbide. The residue contained free carbon, unchanged carbide, and lanthanum sulphate, but no chloride. In this, lanthanum dicarbide differed from calcium carbide which gave a residue of calcium chlorosulphonate. The reaction of lanthanum sesquicarbide with chlorosulphonic acid was slow and incomplete. After 3 hr. at 100°, 40% of the carbide remained unchanged; only hydrogen chloride and sulphur dioxide were evolved and all the carbon in the carbide which had reacted appeared as the free element.

The reaction of the carbides with molten iodine in a sealed tube at 190° provides a further example of differing reactivities. After 5 hr., calcium carbide had reacted completely to give calcium iodide and tetraiodoethylene, C_2I_4, m. p. 187°, whereas the carbides of lanthanum reacted only to the extent of about 40%, the products being yellow crystals of anhydrous lanthanum tri-iodide and free carbon. No iodides of carbon were produced. The smooth reaction of calcium carbide with molten iodine also contrasts with the reaction of this compound with the other halogens. Thus, there was no reaction with liquid chlorine at −35° or with gaseous chlorine at room temperature though at 200° an exothermic reaction occurred which produced calcium chloride and free carbon quantitatively. With molten iodine monobromide at 100° there was 25% reaction to give free carbon, but no carbon–halogen compounds were detected. Liquid bromine, after 6 weeks at room temperature, gave a small amount of hexabromoethane. The reactions of bromine and iodine with calcium carbide confirm the observations by Biesalski and von Eck.[13]

Liquid ammonia was investigated as a typical basic protonic solvent but appeared to be unreactive; for example, lanthanum dicarbide when sealed with liquid ammonia in a glass bomb showed no reaction after three months at room temperature.

Discussion

In addition to the well-known lanthanum dicarbide, the recently reported sesquicarbide [3,4] has been confirmed. There was no evidence for a third carbide, LaC,[9] the

[13] Biesalski and von Eck, *Z. angew. Chem.*, 1928, **41**, 741.

X-ray powder pattern for which suggests that it is an interstitial solution of lanthanum in the dicarbide.

Interpretation of the magnetic-susceptibility measurements involves an estimate of the inherent diamagnetism of the ions present. The two most recent values for the diamagnetic susceptibility of lanthanum sesquioxide (in units of 10^{-6} e.m.u.) are -39 [14] and -46 [11] per mole of $LaO_{1\cdot5}$ and these, together with the accepted value of $-11\cdot25$ for the susceptibility of the oxide ion,[15] lead to values of $-22\cdot1$ and $-29\cdot1$ for the susceptibility of the La^{3+} ion. The mean of these figures is close to the theoretical value of $-27\cdot1$,[15] and this is preferred to the currently accepted value of *ca.* -20.[16] The diamagnetic susceptibility of the acetylide ion, $(C{\equiv}C)^{2-}$, can be calculated from the value for two carbon atoms ($-12\cdot0$) together with a correction for the triple bond and the two negative charges. The value for the triple bond is usually taken to be $+0\cdot8$ but, when two negative charges are also present on the ion, $+0\cdot3$ has been considered more appropriate,[17] leading finally to $-11\cdot7$ for the susceptibility of the acetylide ion. The total correction for the inherent diamagnetism of lanthanum dicarbide is thus $+38\cdot8$, which converts the experimental value of $-7\cdot2$ into a weak paramagnetic susceptibility of $+31\cdot6$. This can reasonably be ascribed to a delocalized valency electron and is negligibly small when compared with the value of *ca.* $+1250$ expected for the bivalent ion La^{2+} (cf. also the values of $+96$ [11] and $+101$ [12] for the paramagnetism of metallic lanthanum which has three delocalized electrons).

Similarly, the corrected value for lanthanum sesquicarbide is $+61\cdot0 \times 10^{-6}$ e.m.u. per mole of $LaC_{1\cdot5}$, again indicating delocalization of the extra 1·5 electrons per lanthanum atom. These conclusions are consistent with the known metallic conductivity of the two carbides [4] and establish the fact that any localization of the supernumerary electrons must be less than 1% of their total concentration. Such localization cannot, therefore, be invoked to explain either the variations in C–C bond length [3] or the complexity of the hydrolysis products.[2,9]

The products obtained by hydrolysis of the carbides might be expected to reflect the presence of the C_2 units in their structure. Calcium carbide yields pure acetylene and it seemed possible that the variety of products reported to be obtained from lanthanum dicarbide resulted from the reducing influence of the extra valency electron. Pettersson [5] first observed that hydrocarbons were evolved but failed to identify them. Moissan [6,18] stated that the products were methane (27·9%), ethylene (1·5%), and acetylene (71·0%) together with a small residue of liquid and solid hydrocarbons, but Damiens,[7] in a more detailed study, reported the presence of hydrogen and the absence of methane. His gaseous products comprised hydrogen (10%), ethane (12·5%), higher paraffins (1·6%), ethylene (6·7%), higher olefins (2·0%), and acetylenes (67·2%). The work of Villelume [8] on the reaction of lanthanum dicarbide with steam at temperatures up to 500° is not comparable with these earlier investigations because of the occurrence of cracking and polymerization reactions amongst the products. The results for 4N-sulphuric acid in Table 1 tend to confirm Damiens's results rather than Moissan's, though there was a trace of methane and no ethane. The production of hydrogen, acetylene, ethylene, and C_4 hydrocarbons and the virtual absence of methane and C_3 hydrocarbons is consistent with the following sequence of reactions: Water molecules are oriented with the oxygen lone-pair electrons towards the La^{3+} ions. Two of each three water molecules then undergo proton transfer to the acetylide ion, the proton from the third molecule combining with an electron from the conduction band to give nascent hydrogen:

$$LaC_2 + 3H{\cdot}OH = La(OH)_3 + C_2H_2 + [H]$$

Most of the acetylene and hydrogen is evolved at this stage, these gases comprising 86·2%

[14] Blanchetais, Thesis, Paris, 1954.
[15] Angus, *Proc. Roy. Soc.*, 1932, *A*, **136**, 569.
[16] Landolt-Börnstein's Tabellen.
[17] Vickery, Sedlacek, and Ruben, *J.*, 1959, 503.
[18] Moissan, *Compt. rend.*, 1898, **127**, 911.

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of the volatile products. However, some of the acetylene is reduced by the nascent hydrogen to ethylene before being evolved, though none is reduced as far as ethane. In addition, partial reduction of acetylene to the vinyl radical, $CH_2{=}CH\cdot$ accounts for the presence of C_4 and the virtual absence of C_3 units in the products. Thus dimerization of the vinyl radical gives buta-1,3-diene, which is the major component of the higher hydrocarbons. However, some of the butadiene is completely reduced to butane, whilst 1,2-addition of hydrogen produces but-1-ene and 1,4-addition gives *cis*- and *trans*-but-2-ene. It is hard to devise a convincing mechanism for the formation of the small amount of carbon dioxide (0·4%). It was not present in the reagents and any explanation must also account for the presence of this gas (1·8%) and carbon monoxide (5·6%) in the hydrolysis products of lanthanum sesquicarbide.

The only reference to the hydrolysis of the sesquicarbide [3] states that about 50% of the gas evolved was acetylene, that the amount of hydrogen liberated was 2½ times that obtained from the dicarbide, and that small amounts of propane, propene, and propyne were formed. Our results with 4N-sulphuric acid were that 36·6% of the evolved gas was acetylene and that, per mole of LaC_2 and $LaC_{1\cdot5}$, the sesquicarbide gave three-fifths of the amount of acetylene and 3·06 times the amount of hydrogen. In addition, small amounts of propane and propene were found, but no propyne. The formation of the C_2 and C_4 hydrocarbons is consistent with the sequence of reactions outlined in the previous paragraph. The presence of 2% of methane may be a consequence of the fact that the C–C bond in the sesquicarbide (1·32 Å) is longer than that in the dicarbide (1·28 Å) and is therefore more easily ruptured during the vigorous reaction. This would also explain the presence of C_3 hydrocarbons ($C_2 + C_1$) and the greater deposit of free carbon from the sesquicarbide.

Reactions with 2N-nitric acid were investigated after it had been found [19] that this reagent was reduced to lower oxides of nitrogen by uranium carbide. The reaction apparently depends on the presence of a metal in a lower oxidation state or the evolution of nascent hydrogen, since calcium carbide yielded only acetylene and a trace of carbon dioxide and did not reduce the nitrate ion. Reduction of nitric acid by lower-valent cations or nascent hydrogen is well known,[20] and, depending on conditions the products may contain nitrogen dioxide, nitric oxide, nitrous oxide, nitrogen, ammonium ions, or hydrazine. However, unless the acid is fairly concentrated or is heated, reaction is normally very slow, though the standard redox potentials for all these reactions are favourable.[21] The reduction of dilute nitric acid in the cold by the carbides of lanthanum is therefore unusually rapid, and the absence of nitrogen and nitrogen–hydrogen compounds from the products is also exceptional. The decrease in the amount of hydrogen and ethylene evolved when nitric rather than sulphuric acid is used for hydrolysis (see Table 1) can be understood in terms of the simultaneous reactions competing for nascent hydrogen. Thus, with dilute sulphuric acid, nascent hydrogen either is evolved as molecular hydrogen or is used to reduce the acetylene to ethylene and other products, but with nitric acid some of the nascent hydrogen is used in reducing the nitrate ions and less is available for reduction of acetylene or evolution of molecular hydrogen.

Secondary reactions also complicate the interpretation of the results obtained with anhydrous sulphuric acid and chlorosulphonic acid. The complexity is illustrated in the case of chlorosulphonic acid by the formation of carbon oxysulphide in addition to free carbon and the oxides of carbon; moreover, despite the release of large volumes of hydrogen chloride, no sulphur trioxide was detected even after evaporation of the excess of chlorosulphonic acid. As with anhydrous sulphuric acid the principal reduction product of the acid was sulphur dioxide.

[19] Toogood, unpublished observations in this laboratory.
[20] Gmelin's "Handbuch der Anorganischen Chemie," Syst. No. 4, "Stickstoff," Verlag Chemie, G.m.b.H., Weinheim/Bergstrasse, 1936.
[21] Latimer, "The Oxidation States of the Elements and Their Potentials in Aqueous Solutions," Prentice-Hall, New York, 1938.

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Experimental

Compounds were handled either in a vacuum-frame or in a glove box which incorporated a wafter motor to circulate the oxygen-free nitrogen atmosphere continuously through a drying train containing phosphorus pentoxide.

Temperatures up to 1200° were obtained by a nichrome-wound silica furnace lagged with asbestos powder. Higher temperatures were obtained by means of a Radyne portable induction furnace. The temperature was measured on a chromel–alumel thermocouple (0—1200°) or by an optical pyrometer (up to 2200°).

X-Ray powder photographs were taken with a Unicam 9 cm. powder camera and copper-K_α radiation. Specimens for magnetic measurements were ground to a fine powder and compressed in a glass tube (5 × 40 mm.) which was closed at each end by glass plates sealed on with picein wax. The susceptibilities were kindly measured by Mr. R. Barnard of the Physics Department.

Lanthanum metal (Johnson Matthey and Co.) was 99·99% pure. Graphite powder was Harwell's grade A. Hydrogen was generated by heating degassed lithium aluminium hydride to 150°. The calcium carbide used in the control experiments was of commercial grade; on the basis of analysis for carbon (acetylene) and calcium (EDTA) the material contained 80% of CaC_2, the main impurity being calcium oxide. Anhydrous sulphuric acid was prepared as previously described.[22] Chlorosulphonic acid (b. p. 150—152°) was purified by fractionation at atmospheric pressure. Iodine monobromide was synthesized directly from the elements.

Lanthanum dihydride was prepared by warming lanthanum in the presence of the correct amount of hydrogen. Absorption was rapid at 40—50° provided that care was taken to avoid the formation of an oxide film on the metal. Samples were then annealed at 300° for 48 hr. before being ground. The hydride was pyrophoric and scrupulous care was necessary to avoid contact with oxygen. Powder photographs confirmed that the compound was face-centred cubic with $a_0 = 5{\cdot}660 \pm 0{\cdot}002$ Å (lit., 5·667,[23] 5·658 [24]).

Lanthanum sesquicarbide was prepared from accurately stoicheiometric amounts of lanthanum hydride and graphite. The two powders were ground together in an agate mortar for 30 min. and then slowly heated to 1000° in a previously degassed silica tube. Hydrogen, which was gradually evolved, was allowed to accumulate in the reaction system until a maximum pressure had been attained. There was no evidence from infrared spectra or molecular-weight determinations for the presence of hydrocarbons in the hydrogen evolved. The sample was then annealed at 1000° at 10^{-5} mm. Lanthanum dicarbide was prepared similarly, after which it was crushed, placed in a degassed graphite crucible, and heated to 2200° under a high vacuum. The sample did not melt but changed colour from dark grey to a metallic yellow, indicating that sintering had occurred.

Reactions of the carbides were carried out on a vacuum-frame which incorporated a constant-volume manometer, Töpler pump, molecular-weight bulbs, and fractionating traps. The reaction system consisted of a tipping unit which could be rotated in a vertical plane about a ground-glass joint to bring the reactants into contact, the unit having previously been charged with known weights of carbide and reagent in the glove box.

Because of the small quantities of material used in each reaction and the complexity of the hydrocarbon mixtures involved, conventional gas analysis would have been both complicated and incapable of identifying all the gases present. A simple method of analysing the various gaseous fractions was therefore developed, by using a combination of infrared spectroscopy and gas–liquid chromatography. Spectra were normally obtained on a Perkin–Elmer Infracord instrument in the range 667—4000 $cm.^{-1}$, but when higher resolution or more accurate wave numbers or intensities were required a Unicam S.P. 100 spectrometer was used. Authentic samples of each gas were obtained and spectra measured at various pressures. Suitable bands were selected and calibration graphs drawn to relate pressure to absorbance (log scale). These graphs normally comprised 6—10 points and were accurately linear. It was found that absorbance varied slightly with the presence of other gases and it was necessary to run calibrations on synthetic mixtures approximating to the composition of the products. In some mixtures absorption bands of two components overlapped to some extent and this necessitated the use of non-overlapping bands in other regions. For example, the strong band in nitrous oxide at

[22] Greenwood and Thompson, *J.*, 1959, 3474.
[23] Holley, Mulford, Ellinger, Koehler, and Zachariasen, *J. Phys. Chem.*, 1955, **59**, 1226.
[24] Stalinski, *Bull. Acad. polon. Sci., Classe III*, 1955, **3**, 613.

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1285 cm.$^{-1}$ is superimposed on the strong acetylene band at 1328 cm.$^{-1}$. Table 3 summarizes the absorption bands selected and the pressure range in which each band was used.

TABLE 3. *Infrared spectra for analysis.*

Gas	Absorption band (cm.$^{-1}$)	Pressure range (mm.)	Gas	Absorption band (cm.$^{-1}$)	Pressure range (mm.)
C_2H_2	729	0—10	CO_2	2349	0—40
	3287	10—60		3660	40—80
	1328	10—100	SO_2	1361	0—20
C_2H_4	949	0—20		1151	20—60
	1444	20—50	COS	2051	0—12
CH_4	1306	0—24	N_2O	2224	0—50
HCl	2960	0—400		2564	0—200
	2886	0—400	NO	1876	0—300
CO	2143	0—400			

The gases listed in Table 3 were obtained from cylinders and purified by fractionation in the vacuum-line or were prepared by standard procedures. Carbon oxysulphide was prepared by adding aqueous potassium thiocyanate to concentrated sulphuric acid.[25]

Gas–liquid chromatographic separations were obtained by using instruments constructed in this Department and we are indebted to Dr. T. F. Palmer and Mr. J. H. Morris for their assistance. The stationary phases used were squalane, dimethylsulpholane, and 2,2′-diethoxydiethyl ether–silver nitrate.

We thank the Atomic Energy Research Establishment, Harwell, for financial support.

THE UNIVERSITY, NOTTINGHAM. [*Received, November 10th,* 1960.]

[25] Bartunck and Barker, *Phys. Rev.*, 1935, **48**, 516.

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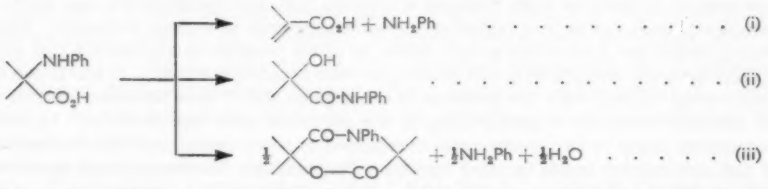
346. *Studies in Pyrolysis. Part XVI.* Pyrolysis of Some Open-chain α-Anilino-carboxylic Acids.*

By J. MCGEE and P. D. RITCHIE.

Several open-chain α-anilino-carboxylic acids (NHPh·CRR′·CO_2H) have been pyrolysed (*ca.* 240°; liquid phase). Where R and R′ are both alkyl, the acids break down by two competitive routes; (i) scission to aniline and an olefinic acid, and (ii) elimination of aniline and water, with formation of a cyclic lactone-lactam. There is no evidence for rearrangement of the anilino-acid to a hydroxy-anilide (contrast Bain and Ritchie [1]). Where R = Me and R′ = Ph, only reaction (i) is observed: where R = R′ = Ph, reaction (i) is structurally precluded, and the complex pyrolysate is best explained as arising from primary elimination of aniline with formation of a cyclic dilactone (benzilide).

Reaction mechanisms are discussed.

BAIN and RITCHIE [1] showed that three homologous 1-anilinocycloalkanecarboxylic acids all break down at *ca.* 250° (liquid phase) by a series of competitive reactions, thus:



* Part XV, *J.*, 1960, 4141.

[1] Bain and Ritchie, *J.*, 1955, 4407.

Reaction (i) increases in importance, and reaction (iii) decreases, as the size of the carbocycle is increased ($C_5 \longrightarrow C_6 \longrightarrow C_7$), while the α-hydroxy-anilide produced by the novel rearrangement (ii) remains a fairly constant minor product throughout. Reaction (i) is probably a primary scission, and reaction (iii) the summation of a primary and a secondary reaction. Reaction (ii) appears [1] to be a direct primary isomerisation; and to study its mechanism further, the work has now been extended from cyclic systems to the open-chain α-anilino-acids (I—IV).

NHPh·CMe$_2$·CO$_2$H (I) NHPh·*CMeEt·CO$_2$H (II) NHPh·*CMePh·CO$_2$H (III) NHPh·CPh$_2$·CO$_2$H (IV)

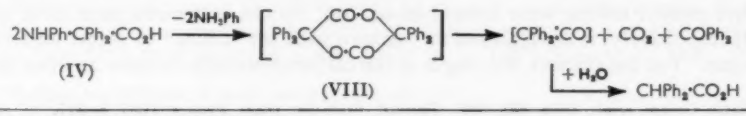
In two of these acids (II, III) the α-carbon atom (*) is dissymmetric; and the intended line of attack was to resolve acids (II) and (III) into their optical antipodes, to pyrolyse these optically active materials, and to find whether detachment of the anilino-group from the dissymmetric carbon atom occurred with or without retention of optical configuration. This stereochemical approach, fruitful in previous studies on various other rearrangements, was here unexpectedly precluded by the observation that the acids (I—IV) gave no detectable quantity of α-hydroxy-anilide on pyrolysis. A separate pyrolysis of the anilide (V), the expected rearrangement product of acid (I), showed it to be stable under the conditions used, so that its absence from the pyrolysate is not due to subsequent thermal breakdown. It seems clear, then, that the novel isomerisation undergone by the three cyclic compounds [1] is not general for all α-anilino-acids.

HO·CMe$_2$·CO·NHPh (V) NHPh·CMe$_2$·CO·NHPh (VI) CH$_2$:CPh·CO·NHPh (VII)

The pyrolysates from acids (I) and (II) contained aniline, water, olefinic acid (see following paragraph), and the curious type of " lactone-lactam " discussed previously.[1,2] In addition, acid (I) gave a trace of the anilino-anilide (VI), presumably by partial condensation of the olefinic acid with aniline from reactions (i) and (iii). Apart, therefore, from the absence of reaction (ii), acids (I) and (II) behave on pyrolysis similarly to their cyclic analogues,[1] even in the increased yield of olefinic acid at the expense of lactone-lactam as molecular weight increases (cf. Table 1). Acid (III), however, yielded only aniline, traces of atropic acid and atropanilide (VII) (the latter presumably by condensation of atropic acid with aniline), and much tar. A reason for the absence of a lactone-lactam is suggested below.

The olefinic acid formed from (II) on pyrolysis is actually a mixture of tiglic and α-ethylacrylic acid. Angelic acid, though a formal possibility, is absent: if formed initially, it must presumably have undergone its known thermal inversion [3] to the more stable geometrical isomer, tiglic acid (cf. an analogous result in the pyrolytic formation of the corresponding olefinic nitriles [4]).

Pyrolysis of acid (IV), which like (III) does not produce a lactone-lactam and is structurally precluded from undergoing primary scission to olefinic acid, yields aniline, benzophenone, carbon monoxide and dioxide, and much tar: also, diphenylacetic acid is obtained from the aqueous alkali used in working-up the products. Previous work [5] on the pyrolysis of benzilide (VIII) suggests that these products are best accounted for by the following reaction, with intermediate formation of the cyclic dilactone (VIII):



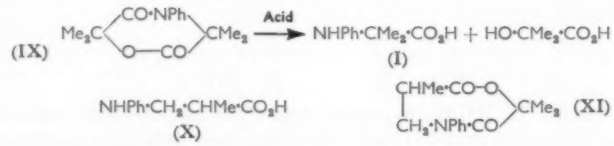
(IV) (VIII)

[2] Plant and Facer, *J.*, 1925, **127**, 2037.
[3] Blaise, *Ann. Chim. Phys.*, 1907, **11**, 111.
[4] Bennett, Deans, Harris, Ritchie, and Shim, *J.*, 1958, 4508.
[5] Hurd, " The Pyrolysis of Carbon Compounds," Chemical Catalog Co., New York, 1929, p. 434.

Vol. 1961, page 1783, line 26. *For* olefinic acid *read* anilino-acid.

It is possible, in addition, that (VIII) may in part break down directly to carbon monoxide and benzophenone (cf. pyrolysis of simple lactides [6]).

The lactone-lactam (IX) (m. p. 116—120°) from acid (I), unlike those from the cyclic anilino-acids,[1] is readily hydrolysed by sulphuric acid at both the ester and the amide linkage, yielding acid (I) itself and the hydroxy-acid:



This confirms the view [1,2] that such lactone-lactam rings are six- rather than seven-membered, though the latter structure is suggested by earlier work by Bischoff and Mintz.[7] These authors ascribed the β-anilino-structure (X) to the acid obtained by them from aniline and ethyl α-bromo-α-methylpropionate, and by von Tiemann [8] from aniline, acetone, and hydrogen cyanide. This is clearly incorrect: the acid must be the α-compound (I), as in fact proposed by von Tiemann: [8] and the pyrolysis product (m. p. 120°) which Bischoff and Mintz [7] obtained from it, and to which they ascribed the seven-membered cyclic structure (XI), is now clearly (IX).

A strong band at 1193 cm.$^{-1}$, assigned [9] to the isopropylidene group, is present in the infrared absorption spectra of the acid (I), the lactone-lactam (IX), and the hydroxy-anilide (V). This provides further evidence for structure (I) rather than (X), the latter lacking the CMe_2 group.

The lactone-lactam (IX) may formally arise from acid (I) either by (*a*) intermolecular elimination of water, followed by intramolecular elimination of aniline, leading to cyclisation (cf. Bain and Ritchie [1]), or (*b*) acylation of unchanged acid (I) by α-methylacrylic acid formed from the latter, followed by cyclisation of the linear intermediate CH_2:CMe·CO·NPh·CMe_2·CO_2H (cf. Bischoff and Mintz [7]). Mechanism (*b*) is now preferred, since it can explain the failure of acids (III) and (IV) to yield a lactone-lactam on pyrolysis. Acid (IV) cannot yield the necessary olefinic acid by elimination of aniline: and although acid (III) can do so, the resulting olefinic acid (atropic acid) here undergoes early pyrolytic conversion [10] into tar, *via* α- and β-isatropic acid.

Pyrolysis of acids (I) and (II) at *ca.* 240° yielded very little gas: and to render the results more comparable with previous studies [1] a few runs were made at *ca.* 540°. At this temperature, acids (I) and (II), and the lactone-lactams formed from them at *ca.* 240°, gave carbon monoxide and carbon dioxide as the major gaseous products, the molar ratio $CO : CO_2$ lying within the range *ca.* 2—5 (cf. Table 2). Bain and Ritchie [1] suggested that the carbon monoxide formed from cyclic anilino-acids may have been due to breakdown of the hydroxy-anilides produced from these by thermal rearrangement (a mode of breakdown observed experimentally [1]): but this cannot be the explanation in the present work, since no such rearrangement is shown by the open-chain anilino-acids. A possible origin for the carbon monoxide lies in the primary formation of lactone-lactams, followed by scission of these to anil, ketone, and carbon monoxide (a breakdown analogous to that of simple lactides,[6] discussed above). This idea, though supported by the fact that acetone and ethyl methyl ketone were formed at *ca.* 540° by the lactone-lactams from acids (I) and (II) respectively, is nevertheless at variance with the failure [1] to detect an anil in the pyrolysate. For the present, the origin of the carbon monoxide remains an open question.

[6] Blaise, *Compt. rend.*, 1904, **138**, 697; Bagard, *Bull. Soc. chim. France*, 1907, **1**, 317.
[7] Bischoff and Mintz, *Ber.*, 1892, **25**, 2326.
[8] von Tiemann, *Ber.*, 1882, **15**, 2042.
[9] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, p. 26.
[10] Fittig and Wurster, *Annalen*, 1879, **195**, 147; McKenzie and Wood, *J.*, 1919, **115**, 828.

Experimental

Apparatus: Procedure: Analytical Methods.—These have been described.[1] Substances were pyrolysed by both the static (Table 1) and the semi-micro (Table 2) flow method.

Table 1. *Results of static pyrolyses (1 hr.).*

Pyrolysand	Acid (I)		Acid (II)	Acid (III)		Acid (IV)
Temp.	220°	240°	240°	240°	180°	240°
Run no.	1	2	4,5 *	6	7	8
Products %: §						
aniline	18·4(35)	18·4(35)	21·5(44)	14·0(36)	7·5(20)	8·3(27)
olefinic acid	—	0·4(1)	1·0(2) †	‡	3·0(5)	Nil
lactone-lactam	17·0(25)	20·0(29)	17·0(24)	Nil	Nil	Nil
anilino-anilide	3·4(4)	—	Nil	Nil	Nil	Nil
tars, waste, losses	61·2	61·2	60·5	86·0	89·5	91·7

* Average of 2 runs. † Mixture of tiglic and α-ethylacrylic acid. ‡ No acid, but trace of atropanilide formed. — Not observed. § Figures in parentheses represent % yield based on conversion into a single constituent: other figures represent % by wt. based on original acid.

Table 2. *Results of semi-micro flow pyrolyses (at 540°, with 300 mg. of pyrolysand).*

Pyrolysand	Acid (I)	Lactone-lactam from (I) *	Acid (II)	Lactone-lactam from (II) †
‡ Gas formed (ml.)	37·0(99)	32·0(59)	34·0(97)	48·0(98)
§ Gas analysis (% by vol.):				
CO	66(58)	63(31)	60(43)	72(62)
CO_2	24(21)	22(11)	30(21)	15(13)
Unsat. hydrocarbons	3	7	5	5
H_2	7	8	5	8
$CO : CO_2$ ratio (moles)	2·8	2·9	2·0	4·8

Acetone (*) and ethyl methyl ketone (†) detected in pyrolysate from lactone-lactam. Figures (‡) in parentheses represent % yield, calculated on assumption that one molecule of acid and one molecule of lactone-lactam yield respectively one and two molecules of gas. Figures (§) in parentheses represent % yield based on conversion into a single constituent.

Preparation of Pyrolysands.—The α-anilino-carboxylic acids (I—III) were prepared by hydrolysing the corresponding 1-anilino-nitriles (made by von Walther and Hübner's method [11]), first to the amide by sulphuric acid (cf. Plant *et al.*[2,12]) and then to the acid by hydrochloric acid. α-Anilino-α-methylpropionic acid (I) (overall yield 17%) had m. p. 184—185° (lit.,[11] m. p. 184—185°). *α-Anilino-α-methylbutyric acid* (II) (10%) had m. p. 144°, forming needles from benzene (Found: C, 68·7; H, 7·9; N, 7·3. $C_{11}H_{15}NO_2$ requires C, 68·4; H, 7·8; N, 7·3%). *α-Anilino-α-phenylpropionic acid* (III) (12%), m. p. 146°, formed needles from carbon tetrachloride (Found: C, 74·3; H, 6·3; N, 6·0. $C_{15}H_{15}NO_2$ requires C, 74·5; H, 6·3; N, 5·8%). α-Anilinodiphenylacetic acid (IV), prepared (6%) as described by Stollé,[13] by the action of aniline on the product formed by treatment of benzilic acid with thionyl chloride, crystallised in needles, m. p. 174°, from benzene (lit.,[13] m. p. 174°). α-Hydroxy-α-methylpropionanilide (V), prepared (16%) by heating α-hydroxy-α-methylpropionic acid with aniline, had m. p. 132—133° (lit.,[14] m. p. 132—133°).

Pyrolysis of Acid (I).—*Run* 1. Pyrolysed in the static system, acid (I) (44 g.: 220°, 1 hr.) yielded on distillation fractions (i) 9·5 g., b. p. 150—200° [containing water, aniline (7·5 g.), and a solid A (0·5 g.), m. p. 116—120°], and (ii) a high-boiling residue (30 g.) which was partly soluble in aqueous sodium carbonate. The aqueous extract, when acidified, yielded 3 g. of crude solid which on recrystallisation gave a further 1·5 g. of material A, m. p. 116—120°; the alkali-insoluble residue was partly soluble in hydrochloric acid. The acidic extract contained aniline (0·5 g.), and when made alkaline gave 1·5 g. of crude α-anilino-α-methylpropionanilide (VI) (m. p. 154—156°, from methanol–water: lit.,[15] m. p. 155°) (Found: C, 75·8; H, 6·8;

[11] von Walther and Hübner, *J. prakt. Chem.*, 1916, **93**, 119.
[13] Betts, Muspratt, and Plant, *J.*, 1927, 1310.
[13] Stollé, *Ber.*, 1910, **43**, 2471.
[14] Tiegerstedt, *Ber.*, 1892, **25**, 2919.
[15] "Dictionary of Organic Compounds," eds. Heilbron and Bunbury, Eyre and Spottiswoode Ltd., London, 1934.

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N, 11·0. Calc. for $C_{16}H_{18}N_2O$: C, 75·6; H, 7·1; N, 11·0%). The acid-insoluble residue, crystallised from benzene–light petroleum, yielded 15 g. of crude solid which on recrystallisation gave 7 g. of pure substance A, as large plates, m. p. 116—120°. (There was also a tarry residue, not studied further.) Substance A was the lactone-lactam (IX), *tetrahydro-2,2,5,5-tetramethyl-3,6-dioxo-4-phenyl-1,4-oxazine* [Found: C, 68·3; H, 7·1; N, 5·6%; *M* (cryoscopic in benzene), 243. $C_{14}H_{17}NO_3$ requires C, 68·0; H, 6·9; N, 5·7%; *M*, 247]. Hydrolysis of this compound (IX) by 4N-sulphuric acid for 25 hr., followed by neutralisation and extraction with ether, yielded acid (I) (mixed m. p.): the liquid remaining after ether-extraction, evaporated to dryness, yielded α-hydroxy-α-methylpropionic acid, m. p. and mixed m. p. 79° (from benzene).

Run 2. A second run was made in an attempt to detect the predicted olefinic acid, not identified in Run 1. Acid (I) (25 g.; 240°, 1 hr.), when pyrolysed and distilled, yielded a liquid (i) (5 g.), b. p. 140—220°, and (ii) a high-boiling residue. Liquid (i) was dissolved in ether and freed from aniline (4·1 g.) by extraction with acid. The ether layer yielded a semi-solid residue, treatment of which with benzene removed α-methylacrylic acid (infrared) and left a resinous residue of (presumably) poly-(α-methylacrylic acid). Product (ii) yielded further aniline (0·5 g.) and pure lactone-lactam (IX), m. p. 116—120° (5 g.): but material (ii) was completely soluble in benzene, unlike the hydroxy-anilide (V), and on examination by infrared spectrometry showed no evidence (*e.g.*, the strong hydroxyl band at 3279 cm.$^{-1}$) that any of this anilide (V) was present.

Run 3. Bain and Ritchie [1] observed that rearrangement of 1-anilinocycloalkanecarboxylic acids is enhanced by prolonged heating at lower temperatures. However, an additional run with acid (I) at 160° for 48 hr. yielded only a large amount of tar, from which a little of the anilino-anilide (VI), m. p. 155—156°, was isolated, but no trace of the α-hydroxy-anilide (V).

Pyrolysis of Acid (II).—*Run* 4. When pyrolysed in the static system, acid (II) (40 g.; 240°, 1 hr.) yielded by distillation a liquid (i) (9·7 g.), b. p. 140—190°, and (ii) a high-boiling residue. Liquid (i), which contained water, was dissolved in ether: treatment with acid removed aniline (7·7 g.), and the residual brown liquid from the ether layer, cooled to 0°, deposited crude tiglic acid which on recrystallisation from hot water gave the pure acid, m. p. and mixed m. p. 58—62° (lit.,[16] m. p. 64°). Product (ii), extracted with hydrochloric acid, yielded further aniline (0·5 g.): the residue, treated with benzene–light petroleum, gave a crude lactone-lactam, m. p. 117° (7 g.), which on recrystallisation yielded *2,5-diethyltetrahydro-2,5-dimethyl-3,6-dioxo-4-phenyl-1,4-oxazine* (5 g.) as plates, m. p. 124—125° [Found: C, 69·8; H, 7·9; N, 5·0%; *M* (cryoscopic in benzene), 270, 279. $C_{16}H_{21}NO_3$ requires C, 69·8; H, 7·7; N, 5·1%; *M*, 275].

Run 5. To find whether tiglic acid was accompanied by either of its isomers (angelic and α-ethylacrylic acid), a further run was made. The total pyrolysate from acid (II) (21 g.; 240°, 1 hr.) was dissolved in ether and extracted first with dilute aqueous sodium carbonate and then with dilute hydrochloric acid. The alkaline extract was divided into two portions. One was oxidised by potassium permanganate: the product was extracted with ether, and contained acetic and propionic acid (gas–liquid chromatography), the latter confirming the presence of α-ethylacrylic acid. The other portion, acidified and extracted with ether, yielded tiglic acid (*ca.* 0·05 g.; mixed m. p.) and a brown liquid (*ca.* 0·1 g.) which yielded no definite information by infrared spectrometry. The acid extract from the original pyrolysate yielded aniline (4·7 g.) and crude lactone-lactam (6 g.), the latter giving 4 g. of pure product, m. p. 124—125°, on recrystallisation. There was a tarry residue. No evidence could be obtained for the presence of either angelic acid or the hydroxy-anilide in the pyrolysate.

Pyrolysis of Acid (III).—*Run* 6. When pyrolysed in the static system, acid (III) (50 g.; 240°, 1 hr.) yielded by distillation (i) a liquid (10 g.) and (ii) a large tarry residue. The liquid (i) consisted of water (*ca.* 1·5 g.) and aniline, the latter being separated (*ca.* 7 g.) by treatment with ether and hydrochloric acid. The acid extract, rendered alkaline, yielded 0·2 g. of atropanilide, m. p. 132° (from methanol–water) (lit.,[18] m. p. 134°) (Found: C, 80·8; H, 5·9; N, 5·9. Calc. for $C_{15}H_{13}NO$: C, 80·8; H, 5·9; N, 6·3%). The tarry residue (ii) was treated with benzene: the only solid product isolated was a trace of α-isatropic acid, m. p. 238° [lit.,[18] m. p. 239° (decomp.)], no atropic acid being detected.

Run 7. Since it is known [18] that a viscous residue of α- and β-isatropic acid is formed on slow distillation of atropic acid, a further run was made at a much lower temperature in an effort to reduce tar formation. The total pyrolysate from acid (III) (40 g.; 180°, 1 hr.) was

[18] von Braun and Rudolph, *Ber.*, 1934, **67**, 269.

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treated with ether, without previous distillation. There was a resinous residue (5·6 g.), from which nothing definite could be isolated; the ether extract, treated with acid, yielded aniline (3 g.), and on further treatment with aqueous sodium carbonate yielded crude atropic acid (1·2 g.), m. p. 106° (from ethanol) (lit.,[15] m. p. 106—107°). (This acid, heated in a test tube and then extracted with benzene, yielded α-isatropic acid, m. p. 238°.) The residual ethereal solution, evaporated to dryness, left a tar: this was dissolved in benzene–light petroleum, and after a week deposited traces of a solid (A), m. p. 204°. Evaporation of the mother-liquor yielded traces of a second solid (B), m. p. 164°. Recrystallised from methanol, these yielded pure nitrogen-free products A, m. p. 206°, and B, m. p. 168° [Found, for A: C, 78·7; H, 5·8; O (direct), 15·7. Found for B: C, 78·7, 78·4; H, 5·8, 6·2; O (direct), 14·3. $C_{7n}H_{6n}O_n$ requires C, 79·2; H, 5·7; O, 15·1%]. Both *substances* were saturated, and yielded no 2,4-dinitrophenylhydrazone: and compound B resisted attenpts at acidic or alkaline hydrolysis. The quantities were too small to permit further study and the compounds remain unidentified.

Pyrolysis of Acid (IV).—*Run* 8. When pyrolysed in the static system, acid (IV) (6 g.; 240°, 1 hr.) yielded a total pyrolysate which on treatment with ether left a resinous residue (0·6 g.). Extracted with hydrochloric acid, the ethereal solution yielded aniline (0·5 g.); extracted with aqueous sodium carbonate, it yielded diphenylacetic acid (0·8 g.), m. p. 148° (mixed m. p.; infrared). The ethereal residue finally yielded a tar, not further studied. There was no evidence for the presence of benzilide (VIII) or a lactone-lactam.

Run 9. A further run was made in a search for benzophenone. The total pyrolysate from acid (IV) (1 g.; 240°, 1 hr.) was taken up in methanol and treated with 2,4-dinitrophenylhydrazine: the appropriate derivative of benzophenone was formed (mixed m. p.).

Pyrolysis of α-Hydroxy-α-methylpropionanilide (V).—Substance (V), when heated at 240° (1 hr.) in the static reactor, remained unchanged.

Semimicro-pyrolyses.—Acids (I) and (II), and the corresponding lactone-lactams, were pyrolysed in the semimicro-apparatus (Table 2).

New Infrared Data.—The following are the principal absorption bands of the compounds studied.

Acid (I): 1618s, 1495m, 1404s, 1359s, 1218m, 1193m, 1156m, 1030m, 917m, 897m, 819m, 806m, 782m, 741s, 693s cm.$^{-1}$ (Assignments: 1618 cm.$^{-1}$, CO_2^-; 1193 cm.$^{-1}$, CMe_2 [9]).

Acid (II): 1616s, 1486m, 1391s, 1359s, 1325m, 1305w, 1284m, 1183w, 1145m, 1135w, 1025m, 885m, 797m, 763w, 735s, 692s cm.$^{-1}$ (Assignment: 1616 cm.$^{-1}$, CO_2^-).

Acid (III): 1650s, 1613s, 1558w, 1495s, 1389s, 1361s, 1511w, 1282w, 1258w, 1208w, 1183w, 1156w, 1130w, 1075w, 1029m, 912w, 881m, 797w, 766w, 739s, 694s cm.$^{-1}$ (Assignment: 1650 cm.$^{-1}$, acid C=O; 1613 cm.$^{-1}$, CO_2^-; 1558 cm.$^{-1}$, benzene ring).

Acid (IV): 1626s, 1493sh, 1326s, 1279sh, 1220w, 1183sh, 1170w, 1156sh, 1081w, 1026sh, 985w, 905w, 890w, 833w, 785w, 782w, 746s, 722s, 687s cm.$^{-1}$ (Assignment: 1626 cm.$^{-1}$, CO_2^-).

Lactone-lactam from acid (I): 1745s, 1661s, 1595w, 1490w, 1406s, 1389sh, 1305s, 1250m, 1220m, 1190m, 1147s, 1053m, 759s, 702s cm.$^{-1}$.

Lactone-lactam from acid (II): 1727s, 1667s, 1590m, 1495m, 1437m, 1416s, 1340s, 1309s, 1259s, 1233s, 1211m, 1176m, 1156s, 1130s, 1080m, 1070m, 1036s, 1030sh, 1022 sh, 1000m, 976w, 961m, 855m, 848sh, 812w, 806w, 761s, 735w, 702s cm.$^-$ (Assignments: 1745, 1727, 1667, 1661cm.$^{-1}$, lactone C=O; 1595, 1590 cm.$^{-1}$, benzene ring).

Hydroxy-anilide (V): 3279s, 1667s, 1608s, 1555s, 1504w, 1490w, 1449s, 1416w, 1361w, 1333w, 1325m, 1235m, 1190s, 1167sh, 1156s, 976s, 926m, 908m, 761s, 751s, 693s cm.$^{-1}$ (Assignments: 3279 cm.$^{-1}$, OH; 1667 cm.$^{-1}$, NH).

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347. *Alkoxy-radicals. Part I. The Kinetics of Thermal Decomposition of Dibenzyl Hyponitrite in Solution.*

By S. K. Ho and J. B. de Sousa.

The rate of decomposition of dibenzyl hyponitrite in various organic solvents is decreased by radical inhibitors, indicating the presence of induced decomposition. At a sufficiently high concentration of inhibitor, such as *p*-benzoquinone or styrene, the rate is of the first order and independent of inhibitor concentration.

At maximum inhibition the rate is relatively insensitive to the nature of the solvent, indicating that the decomposition is by a non-ionic mechanism. An average value of $24{\cdot}94 \pm 0{\cdot}24$ kcal. mole^{-1} was obtained for the activation energy of decomposition, and the frequency factor, *ca.* 10^{13} sec.$^{-1}$, falls within the range for unimolecular reactions.

Besides nitrogen, products found in various solvents were benzaldehyde and benzyl alcohol. The constancy of the yield of benzaldehyde at high dilutions indicates a " cage " disproportionation of benzyloxy-radicals formed in pairs.

Evidence for the recombination of benzyloxy-radicals is considered, and a preliminary study of the effect of dibenzyl hyponitrite on the polymerisation of methyl methacrylate reported.

Studies have been made on alkoxy-radicals derived from the pyrolysis and/or photolysis of alkyl nitrites and nitrates, dialkyl peroxides, and carboxylic acid esters.[1] The present work concerns the reactions of alkoxy-radicals formed in the decomposition of dialkyl and diaralkyl hyponitrites.

The lower dialkyl hyponitrites were first prepared by Zorn,[2] and the dibenzyl ester by Hantzsch and Kaufmann.[3] Partington and Shah [4] found several such esters to decompose according to the scheme (A) initially proposed by Zorn.

$$R{\cdot}CH_2{\cdot}O{-}N{=}N{-}O{\cdot}CH_2R \longrightarrow N_2 + R{\cdot}CHO + R{\cdot}CH_2{\cdot}OH \quad \text{(A)}$$

In 1956, the thermal decomposition of diethyl hyponitrite, studied mass-spectrometrically,[5] was found to occur at a lower temperature than that of di-t-butyl peroxide, suggesting a lower energy of activation for the decomposition of the former. The products above 250° were nitrogen, formaldehyde, and the methyl radical, which are accounted for by reactions (1) and (2) (R = Me):

$$R{\cdot}CH_2{\cdot}O{\cdot}N{=}N{\cdot}O{\cdot}CH_2R \longrightarrow 2R{\cdot}CH_2O{\cdot} + N_2 \quad \text{(1)}$$

$$R{\cdot}CH_2{\cdot}O{\cdot} \longrightarrow R{\cdot} + CH_2O \quad \text{(2)}$$

$$Ph{\cdot}CH_2{\cdot}O{\cdot} \longrightarrow Ph{\cdot}CHO + H{\cdot} \quad \text{(3)}$$

$$2Ph{\cdot}CH_2{\cdot}O{\cdot} \longrightarrow Ph{\cdot}CH_2{\cdot}OH + Ph{\cdot}CHO \quad \text{(4)}$$

$$2Ph{\cdot}CH_2{\cdot}O{\cdot} \longrightarrow Ph{\cdot}CH_2{\cdot}O{\cdot}O{\cdot}CH_2Ph \quad \text{(5)}$$

$$R{\cdot} + Ph{\cdot}CH_2{\cdot}O{\cdot}N{=}N{\cdot}O{\cdot}CH_2Ph \longrightarrow Ph{\cdot}\dot{C}H{\cdot}O{\cdot}N{=}N{\cdot}O{\cdot}CH_2Ph + RH \quad \text{(6)}$$

$$Ph{\cdot}\dot{C}H{\cdot}O{\cdot}N{=}N{\cdot}O{\cdot}CH_2Ph \longrightarrow Ph{\cdot}CHO + N_2 + Ph{\cdot}CH_2{\cdot}O{\cdot} \quad \text{(7)}$$

$$Ph{\cdot}CH_2{\cdot}O{\cdot} + HS \longrightarrow Ph{\cdot}CH_2{\cdot}OH + S{\cdot} \quad \text{(8)}$$

[R· = Ph·CH$_2$·O· or S· (solvent radical).]

[1] Steacie, " Atomic and Free Radical Reactions," Reinhold, New York, 1954, Vol. I, p. 232; Raley, Rust, and Vaughan, *J. Amer. Chem. Soc.*, 1948, **70**, 88, 1336; Bell, Rust, and Vaughan, *ibid.*, 1950, **72**, 337, 338; Seubold, Rust, and Vaughan, *ibid.*, 1951, **73**, 18; Gray and Williams, *Trans. Faraday Soc.*, 1959, **55**, 760; *Chem. Rev.*, 1959, **59**, 239; Luft, *Z. Elektrochem.*, 1956, **60**, 94; Wijnen, *J. Chem. Phys.*, 1958, **28**, 271.

[2] Zorn, *Ber.*, 1878, **11**, 1306.

[3] Hantzsch and Kaufmann, *Annalen*, 1896, **292**, 317.

[4] Partington and Shah, *J.*, 1932, 2593.

[5] Lossing and de Sousa, unpublished work, Ottawa, 1956.

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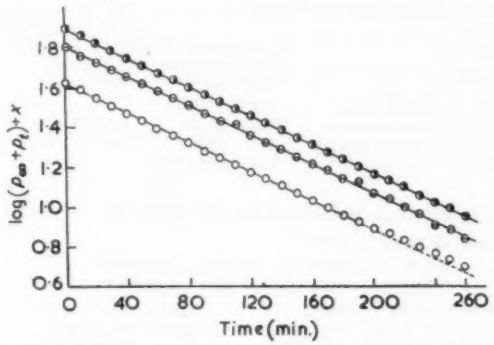
Reaction (2), suggested by Walsh,[6] has been confirmed by Lossing and de Sousa [7] who decomposed various n-alkyl nitrites in a flow system and found that the alkoxy-radicals formed decompose giving mainly formaldehyde and an alkyl radical. Dibenzyl hyponitrite had been used as a radical catalyst in the polymerisation of methyl methacrylate [8] and in the Wohl–Ziegler bromination reaction.[9] It thus appears that, in solution as well as in the gas phase, decomposition of hyponitrite esters follows a radical path.

In the present work the dibenzyl ester has been selected for study as it is a crystallisable solid whereas the dialkyl esters are liquids difficult to purify.

Results

In earlier studies [2,4] decomposition was carried out in absence of solvent, or in water or aqueous alcohol where solvolytic reactions may well occur. It is then of importance to identify the products in other solvents and it is now found that benzaldehyde, benzyl alcohol, and nitrogen are formed in a variety of aromatic solvents and in cyclohexane. A quantitative

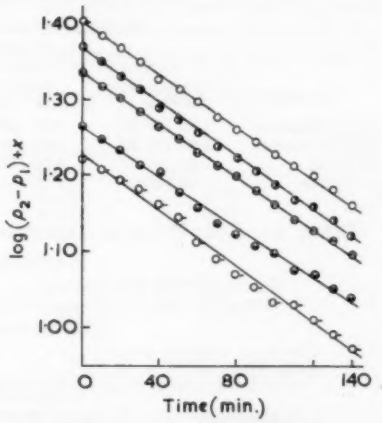
FIG. 1. *Decomposition of dibenzyl hyponitrite* (0·05M) *in chlorobenzene at* 45° *with and without inhibitor* (*infinity reading plot*).



○ Without inhibitor ($x = 0$). ⊖ With 0·03M-styrene ($x = 0·3$). ◑ With 0·8M-*p*-benzoquinone ($x = 0·3$).

(x is an arbitrary displacement, for clarity.)

FIG. 2. *Decomposition of dibenzyl hyponitrite* (*various concentrations in nitrobenzene at* 34·95° *in the absence of inhibitor* (*Guggenheim plot*).



○ 0·075M ($x = 0·5$). ◑ 0·050M ($x = 0$). ⊖ 0·30M ($x = 0$). ◒ 0·010M ($x = 0$). ○– 0·0075M ($x = 0$).

yield of nitrogen, estimated volumetrically, was reported by Partington and Shah.[4] In our hands fresh solutions, prepared at room temperature, immediately begin to evolve nitrogen which was obtained in yields of *cf.* 95%. Some loss of nitrogen occurred during vacuum-degassing in the manometer vessel before measurement. The nitrogen was free from formaldehyde which might possibly arise by reaction (2) (R = Ph). A further complication due to the formation of hydrogen atoms in step (3) is considered unlikely on thermochemical grounds. Gray and Williams [1] cite for aryl-substituted alkoxy-radicals a value of 3—4 kcal. mole^{-1} for [D(C–H)–D(C–Ar)] where Ar is an aryl group, and consequently, the benzyloxy-radical should preferentially decompose by reaction (2). Since the absence of reaction (2) has been established experimentally in the range of our working temperatures, it appears unlikely that reaction (3) will occur to a significant extent.

[6] Walsh, *Trans. Faraday Soc.*, 1946, **42**, 269.
[7] Lossing and de Sousa, *J. Amer. Chem. Soc.*, 1959, **81**, 281.
[8] Harris, Marshall, and Jarrett, *Nature*, 1947, **159**, 843.
[9] Hasbruck, Spielman, and Hamlin, U.S.P. 2,727,906/1955.

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Kinetic measurements were made by following the rate of evolution of nitrogen by a manometric method similar to those employed by others.[10] The method involved vacuum-degassing, and rate measurements were limited to solvents which could be frozen in carbon dioxide–acetone, liquid air not being available. The solvents used were cyclohexane, benzene, chlorobenzene, bromobenzene, nitrobenzene, *o*-nitrotoluene, styrene, *p*-xylene, and carbon tetrachloride. First-order plots of the rate of evolution of nitrogen in all the solvents mentioned (with the exception of carbon tetrachloride) are linear to at least 75% of complete decomposition and thereafter begin to curve very gradually as shown in Fig. 1. Values of the first-order rate constant k obtained from the linear portion of the plot are reproducible within 3%.

The values of k at 40° are shown in Table 1. The highest are for the halogenated benzenes and the lowest for the nitro-compounds, which is consistent with their behaviour as retarders of radical-chain reactions. Styrene, which has been used by Swain *et al.*[11] as an inhibitor in the decomposition of dibenzoyl peroxide in solution, shows an intermediate value at this temperature. The rate constant for the decomposition of dibenzyl hyponitrite in styrene was obtained by Guggenheim's method as the styrene became highly viscous during the later stages of decomposition and an accurate value of the final pressure of nitrogen could not be obtained.

The values of k over a ten-fold range of concentrations for several solvents are given in Table 2. There appears to be a trend towards lower rate constants with decreasing concentration, though the variations are within the margin of experimental error. The values marked

TABLE 1. *Rates of decomposition of dibenzyl hyponitrite in different solvents.*

(Temperatures in °c are enclosed in parentheses)

	k, in absence of *p*-benzoquinone (10^{-4} sec.$^{-1}$)	k_d, in presence of 0·8M-*p*-benzoquinone (10^{-4} sec.$^{-1}$)		k, in absence of *p*-benzoquinone (10^{-4} sec.$^{-1}$)	k_d, in presence of 0·8M-*p*-benzoquinone (10^{-4} sec.$^{-1}$)
Chlorobenzene	1·62 (39·95)	1·42 (40·00)	Cyclohexane ...	1·63 (39·95)	—
Bromobenzene	1·62 (39·90)	1·43 (40·00)	Nitrobenzene ...	1·28 (39·90)	1·26 (40·00)
Benzene	1·47 (40·00)	1·38 (40·00)	*o*-Nitrotoluene	1·29 (39·90)	1·28 (39·95)
p-Xylene	1·48 (40·00)	1·38 (40·00)	Styrene	1·52 (40·00)	—

TABLE 2. *Effect of initial concentration of dibenzyl hyponitrite on rate of decomposition.*

In chlorobenzene at 34·95° ± 0·05°.

Concn. of ester (M)	0·075	0·050	0·030	0·0098 *
Rate, 10^4k (sec.$^{-1}$)	0·85	0·82	0·80	0·84 *

In nitrobenzene at 34·95° ± 0·05°.

Concn. of ester (M)	0·075	0·050	0·030	0·010 *	0·0075 *
Rate, 10^4k (sec.$^{-1}$)	0·66	0·67	0·66	0·63 *	0·70 *

In cyclohexane at 34·90° ± 0·05°.

Concn. of ester (M).....	0·074	0·050	0·030	0·0098 *	0·0074 *
Rate, 10^4k (sec.$^{-1}$)	0·86	0·85	0·82	0·84 *	0·64 *

TABLE 3. *Effect of concentration of* p*-benzoquinone on rates of decomposition of dibenzyl hyponitrite in chlorobenzene at* 34·95° ± 0·05°.

(0·05M-Dibenzyl hyponitrite throughout.)

p-Benzoquinone (M)	0	0·10	0·16	0·25	0·34	0·38	0·42	0·50	0·55
Half-life, $t_{\frac{1}{2}}$ (hr.).....	2·32	2·39	2·45	2·52	2·52	2·62	2·65	2·64	2·68
p-Benzoquinone (M)	0·62	0·68	0·75	0·80	0·88	1·00	1·12	1·25	1·50
Half-life, $t_{\frac{1}{2}}$ (hr.).....	2·70	2·67	2·77	2·71	2·79	2·75	2·80	2·75	2·76

with an asterisk are for the highest dilutions where the plots are slightly wavy (Fig. 2). At these low pressures of nitrogen the method appears to be not so reliable, possibly owing to inadequate stirring (see Experimental section).

The possible presence of an induced chain reaction indicated by the lower rates in retarding solvents such as nitrobenzene and *o*-nitrotoluene is further supported by inhibitory effects in presence of styrene, chloranil, and *p*-benzoquinone. In all solvents the effect of inhibitors

[10] DeTar, *J. Amer. Chem. Soc.*, 1955, **77**, 2013; 1956, **78**, 3911; Bartlett and Jones, *ibid.*, 1957, **79**, 2153; Tobolsky and Van Hook, *ibid.*, 1958, **80**, 779.

[11] Swain, Stockmayer, and Clark, *J. Amer. Chem. Soc.*, 1950, **72**, 5426.

was to decrease the rate of nitrogen evolution and to increase the half-life. Table 1 shows the effect of 0·8M-*p*-benzoquinone on the rate constant in various solvents: its inhibitory effect varied, being greatest with the halogenobenzenes and very slight in nitrobenzene and *o*-nitrotoluene. The decomposition thus shows features in common with that of dibenzoyl peroxide in solution although, as will appear, the amount of induced decomposition in the case of dibenzyl hyponitrite is less.

To measure the rate of the spontaneous decomposition the use of inhibitors to suppress the induced reaction has been adopted and solutions of styrene and quinones were used, following the work of others.[11,12] The rates of decomposition of dibenzyl hyponitrite in solution at maximum inhibition by both styrene or *p*-benzoquinone are close. Thus the values for k at 40° in chlorobenzene is $1{\cdot}42 \times 10^{-4}$ sec.$^{-1}$ with *p*-benzoquinone and $1{\cdot}40 \times 10^{-4}$ sec.$^{-1}$ with styrene as inhibitors. Styrene was, however, more difficult to handle and *p*-benzoquinone was used for more detailed studies. The use of chloranil and phenanthraquinone was also abandoned as they did not have the required range of solubility.

Table 3 shows that an increase in the concentration of *p*-benzoquinone decreases the half-life of dibenzyl hyponitrite in 0·05M-solution in chlorobenzene until about 0·7M-concentration, thereafter being without effect; the k_d values obtained by using the " final " pressure and by the Guggenheim method agreed within 3%. The first-order plot is linear throughout the range of accurate observation (90% of total decomposition). Over a ten-fold variation of concentration in dibenzyl hyponitrite in presence of 0·8M-*p*-benzoquinone the rates show no concentration-dependence below a 0·05M-concentration of dibenzyl hyponitrite (Table 4).

Values of the spontaneous rates of decomposition in various solvents were therefore evaluated at 0·8M- and 0·05M-concentration in *p*-benzoquinone and dibenzyl hyponitrite respectively (Tables 1, 5). Specimen first-order plots for five temperatures are detailed in Fig. 3.

TABLE 4. *Decomposition of dibenzyl hyponitrite in presence of* 0·8M-p-*benzoquinone at* 34·95° ± 0·05°.

In chlorobenzene		In nitrobenzene	
Ester (M)	10^4k_d (sec.$^{-1}$)	Ester (M)	10^4k_d (sec.$^{-1}$)
0·074	0·72	0·0098	0·68
0·050	0·71	0·0073	0·77
0·030	0·75		
	In nitrobenzene		
Ester (M)	10^4k_d (sec.$^{-1}$)	Ester (M)	10^4k_d (sec.$^{-1}$)
0·075	0·66	0·010	0·60
0·050	0·62	0·0074	0·62
0·030	0·61		

TABLE 5. *Rates of decomposition of dibenzyl hyponitrite in different solvents.*

Solvent	10^4k_d (sec.$^{-1}$)	10^4k_d (sec.$^{-1}$)
Chlorobenzene	0·18 (25·00)	0·71 (35·00)
Bromobenzene	0·18 (25·00)	0·76 (34·95)
Benzene	0·20 (25·00)	0·70 (34·95)
p-Xylene	0·21 (24·95)	0·72 (35·00)
Cyclohexane	0·24 (24·95) *	0·78 (34·90) †
	0·18 (24·95) †	— —
Nitrobenzene	0·17 (24·95)	0·65 (34·95)
o-Nitrotoluene	0·18 (24·95)	0·67 (35·00)
Styrene	0·20 (24·90) *	0·81 (35·00) *

A typical plot of the energy of activation is shown in Fig. 4 and a complete summary is given in Table 6. The frequency factors in all solvents range from 10^{13} to 10^{14} sec.$^{-1}$, typical of unimolecular reactions. The low activation energy of *ca.* 25 kcal. mole^{-1} is in conformity with the concerted rupture of the two O–N bonds yielding the stable nitrogen molecule. The scheme in which two bonds are broken simultaneously with the formation of the N–N triple bond as a source of compensating energy is similarly considered to operate in the decomposition of azoalkanes [13] and in the α-phenylated azoalkanes.[14] In the present study it was confirmed

[11] Bartlett, Hammond, and Kwart, *J. Amer. Chem. Soc.*, 1958, **80**, 5313.
[13] Semenov, " Some Problems of Chemical Kinetics and Reactivity," Pergamon Press, London, 1958, Vol. I, p. 270.
[14] Cohen and Wang, *J. Amer. Chem. Soc.*, 1955, **77**, 4510.

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that polymerisation of methyl methacrylate as well as styrene was catalysed by dibenzyl hyponitrite. The effect of quinones, nitro-compounds, and styrene on the rate of decomposition of dibenzyl hyponitrite in solution indicates that, at least in part, the decomposition proceeds

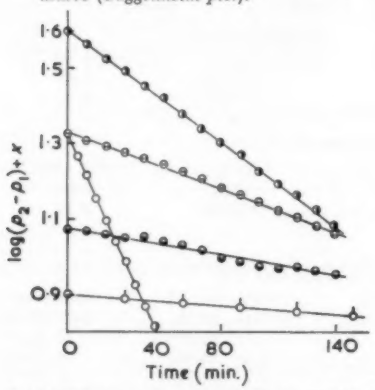
TABLE 6. *Activation energy (E_a in kcal. mole^{-1}) of decomposition of dibenzyl hyponitrite in different solvents in presence of* 0·8M-p-*benzoquinone.*

Solvent	E_a	Average E_a	Solvent	E_a	Average E_a
Chlorobenzene	24·97	25·11	Cyclohexane †	25·69 †	25·33 †
	25·44			24·96 †	
	24·61		Nitrobenzene	24·52	24·56
	25·43			24·60	
Bromobenzene	25·05	25·13	*o*-Nitrotoluene	24·58	24·00
	25·22			23·41	
Benzene	24·59	24·96	Syrene *	24·57 *	24·90 *
	25·33			25·22 *	
p-Xylene	25·35	25·40			
	25·45				

* Without any *p*-benzoquinone. † In presence of 0·025M-*p*-benzoquinone only.

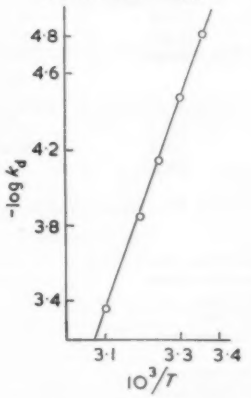
by spontaneous decomposition into radicals which may induce chains in absence of inhibitors. In addition, the relative insensitivity of the spontaneous rates in various solvents from non-polar cyclohexane and benzene through the increasingly polar solvents bromobenzene, chlorobenzene, nitrobenzene, and *o*-nitrotoluene is that to be expected of a non-ionic reaction. In

FIG. 3. *Decomposition of dibenzyl hyponitrite* (0·05M) *in chlorobenzene in presence of* 0·8M-p-*benzoquinone at different temperatures (Guggenheim plot).*



○ 49·45° ($x = 0$). ◑ 40·0° ($x = 0{\cdot}15$).
⊖ 35·0° ($x = 0$). ◒ 30·0° ($x = 0$).
○ 25° ($x = 0$).

FIG. 4. *Decomposition of dibenzyl hyponitrite* (0·05M) *in chlorobenzene in presence of* 0·8M-p-*benzoquinone at different temperatures (determination of activation energy).*



fact, the most highly polar solvents, nitrobenzene and *o*-nitrotoluene, show the lowest rate. This is in contrast to the thermal decomposition of azobisisobutyronitrile at 62·5° where nitrobenzene shows the highest rate, values of $10^5 k_d$ in benzene, nitrobenzene, and chlorobenzene being 1·18, 1·79, and 1·54 sec.$^{-1}$, respectively.

The amount of induced reaction appears to be less than in the case of dibenzoyl peroxide. Thus at 35° the half-life of a 0·05M-solution of dibenzyl hyponitrite is increased from 2·32 hr. in absence of inhibitor to 2·75 hr. at maximum inhibitor, an increase of 18·5%. For dibenzoyl peroxide at 80° the half-life is increased from 1·08 hr. to 1·75 hr., an increase of 62%.[11] Comparison with azobisbutyronitrile [15] and dibenzoyl peroxide [11] shows a narrower range of variation

[15] Hammond, Sen, and Boozer, *J. Amer. Chem. Soc.*, 1955, **77**, 3244.
[16] Nozaki and Bartlett, *J. Amer. Chem. Soc.*, 1946, **68**, 1686.

for k_d values for dibenzyl hyponitrite in several solvents: compare the data in Table 1 with those in the preceeding paragraph and the following values of $10^5 k_d$ for the thermal decomposition of dibenzoyl peroxide at 80° in benzene, cyclohexane, and nitrobenzene, which are 3·28, 6·36, and 3·28 sec.$^{-1}$, respectively.

Discussion

The details of the reaction must be viewed from the quantitative and qualitative aspects of the products and in terms of the processes (1)—(8). Although the evidence indicates a radical chain, it is possible that the reaction, at least in part, proceeds through a molecular mechanism. In the decomposition of azobisisobutyronitrile where the azo-group is also eliminated in the form of molecular nitrogen, a possible transition state has been considered which is similar to a *cis*-azo-compound and the mechanism then is assumed to involve a *trans*- to *cis*-transformation. Hammond *et al.*[15] consider such a mechanism unlikely as the efficiency of radical production in solution appears to vary more with the nature of the solvent than does the rate of decomposition.

Evidence for a *trans*-configuration of the hyponitrite ion has been adduced on the basis of Raman and infrared spectra.[17] Hunter and Partington[18] assigned a *trans*-configuration to dibenzyl hyponitrite on the basis of dipole-moment measurements. Known energies of activation for conversion of *cis*- into *trans*-isomers for aromatic azo-compounds[19] are of the order of 25 kcal. mole^{-1}. In these compounds as well as in ethylenic compounds the energy of the transition state is lowered by possibilities of conjugation with the phenyl group: thus, Wheland and Chen[20] calculated a value of 33 kcal. mole^{-1} for the conversion of *cis*- into *trans*-di-imide (H–N=N–H). Dibenzyl hyponitrite has a non-conjugated azo-linkage and the energy of activation for *cis*- into *trans*-conversion should therefore be higher than for conjugated azo-compounds. Further, the activation energy for the *trans*- to *cis*-change must include the enthalpy difference between the two isomers in the ground state. For the azobenzenes[21] this is of the order of 10 kcal. mole^{-1}. Thus it appears that such a mechanism of decomposition for dibenzyl hyponitrite would involve energies in excess of the energy for decomposition of 25 kcal. mole^{-1}. The existing evidence appears not to support a molecular mechanism occurring to any significant extent and it may be envisaged that decomposition occurs by a concerted rupture of the two O–N bonds in a *trans*-configuration, with the elimination of nitrogen and the formation of two benzyloxy-radicals in a solvent cage.[22]

The products, benzaldehyde and benzyl alcohol, have been accounted for by Gray and Williams[1] as resulting from the disproportionation of benzyloxy-radicals which may be derived from the same (cage disproportionation[22]) or from different parent molecules. In addition, benzyl alcohol may arise by hydrogen-abstraction from solvent, reaction (8), and from the parent hyponitrite, reactions (1 + 4), which gives a radical which may decompose into the benzyloxy-radical, nitrogen, and benzaldehyde. This is analogous to the decomposition of radicals formed by hydrogen abstraction from dibenzyl ethers studied by Huang and Si-Hoe:[23]

$$\mathrm{Ph{\cdot}\dot{C}H{\cdot}O{\cdot}CH_2Ph} \longrightarrow \mathrm{Ph{\cdot}CHO} + \mathrm{Ph{\cdot}CH_2{\cdot}}$$

Benzaldehyde may be produced by means of a cage or non-cage disproportionation and by the induced reaction. The induced reaction and the non-cage disproportionation are second-order reactions and their importance would depend on the initial concentration of dibenzyl hyponitrite, whereas the cage disproportionation has a probability independent of the concentration of dibenzyl hyponitrite. In solution in cyclohexane, yields of benzaldehyde can be determined by spectrophotometry. Solutions of dibenzyl hyponitrite of

[17] Kuhn and Lippincott, *J. Amer. Chem. Soc.*, 1956, **78**, 1820.
[18] Hunter and Partington, *J.*, 1933, 309.
[19] Le Fèvre and de Sousa, *J.*, 1955, 3154.
[20] Wheland and Chen, *J. Chem. Phys.*, 1956, **24**, 67.
[21] Corruccini and Gilbert, *J. Amer. Chem. Soc.*, 1939, **61**, 2925.
[22] Franck and Rabinowitsch, *Trans. Faraday Soc.*, 1934, **30**, 120.
[23] Huang and Si-Hoe, *Proc. Chem. Soc.*, 1957, 354.

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various concentrations were sealed in degassed ampoules and decomposed at 30°, 35°, and 40° in thermostats until no further yield of nitrogen was observable and for a minimum period of at least 15 half-lives. Analyses for benzaldehyde were carried out by using its

TABLE 7. *Percentage yield of benzaldehyde in the decomposition of dibenzyl hyponitrite in cyclohexane.* [Percentage yield = 100 × concn. of Ph·CHO found/concn. of $(CH_2Ph)_2N_2O_2$.]

Concn. (M)	Ph·CHO (%)			Concn. (M)	Ph·CHO (%)			Concn. (M)	Ph·CHO (%)		
of soln.	40·0°	35·0°	30·0°	of soln.	40·0°	35·0°	30·0°	of soln.	40·0°	35·0°	30·0°
0·1000	65·34			0·00399	53·50				50·89		
0·0500	65·58			0·00351	52·91	53·48	53·21	0·000762		49·60	50·12
0·0100	57·38			0·00301	53·95	52·46	53·27	0·000500	50·29		
0·00748	55·80			0·00198	53·02	50·77	53·02	0·000492			49·60
0·00500	53·15			0·00149	51·29	50·08	51·56	0·000103	50·29		51·05
0·00453	53·47	55·44	55·44	0·00100	50·55	49·95	49·74				

ultraviolet absorption maximum at 285·5 mμ. At this wavelength benzaldehyde absorbs strongly (ε 1000) whereas absorption by benzyl alcohol (ε 2) is negligible. The yields of benzaldehyde over a thousand-fold range of concentration are given in Table 7. At 40° the yield drops from 65% at 0·1M to 50% at 0·001M and remains stationary thereafter to at least 0·0001M. The high and constant yield of benzaldehyde at high dilutions strongly supports a cage disproportionation. For the decomposition of δ-phenylvaleryl peroxide in carbon tetrachloride over a 600-fold range in concentration, DeTar and Weis [24] found that at 55° cage processes accounted for 55% of the reaction. As cage-radical reactions are not regarded as susceptible to inhibition, the yield of benzaldehyde is being checked in presence of radical inhibitors. The efficiency of radical production is being examined with the aid of inhibitors such as quinones, diphenylpicrylhydrazyl, and iodine concurrently with studies of efficiencies in the polymerisation of monomers. The yield of benzaldehyde is independent of temperature at high dilutions in the range 30—40° within the range of experimental error, there being here no significant difference between the activation energies for diffusion out of a cage and disproportionation in a cage, both of which should be small.

No example of dimerisation of alkoxy-radicals is available, except for the cases of the cumyloxy-radical cited by Gray and Williams [1] which cannot undergo disproportionation by transfer of a hydrogen atom (as in the benzyloxy-radical) so that it may dimerise. Solutions of dibenzyl hyponitrite decomposed at low temperatures did not give tests for

TABLE 8. *Determination of benzaldehyde (in duplicate) for* 0·00076M-*solutions of dibenzyl hyponitrite in cyclohexane after decomposition.*

	Optical density			
	Sample A	Sample B	Average	Ph·CHO (%)
96 hr. at 35°	0·378	0·374	0·376	49·01
96 + 65 hr. at 35°.....	0·379	0·373	0·376	49·01
96 hr. at 35° + 65 hr. at 100°	0·419	0·420	0·420	54·74

peroxide, and only benzaldehyde and benzyl alcohol were isolated. Quantitative spectroscopical studies indicated erratic yields of benzyl alcohol and the total yield of benzaldehyde and the alcohol exceeds the theoretical: the reaction may proceed by dimerisation and then a reversible fission of the dibenzyl peroxide. An approximate estimate of the contribution of the reverse of reaction (5) to the rate of formation of benzaldehyde could be made if the rate of decomposition of dibenzyl peroxide were available. This does not appear to have been studied, though the related di-α-cumyl peroxide decomposes [25] in cumene by a first-order non-chain mechanism according to the rate equation $k = 4{\cdot}31 \times 10^{14} \exp(-34{,}500/RT)$ sec.$^{-1}$.

[24] DeTar and Weis, *J. Amer. Chem. Soc.*, 1956, **78**, 1820.
[25] Bailey and Godin, *Trans. Faraday Soc.*, 1956, **52**, 68.

In solution, di-α-cumyl peroxide would have a half-life of $1{\cdot}26 \times 10^6$ hr. at 35° (by extrapolation),[25] whereas the half-life of dibenzyl hyponitrite at 35° in cyclohexane is 2·46 hr. Thus it appears that at 35° benzaldehyde should be formed directly by disproportionation of benzyloxy-radicals generated by the parent hyponitrite.

A study of the rate of appearance of benzaldehyde at 35° in cyclohexane solutions in the absence of oxygen using the 285·5 mμ maximum was attempted. The optical density

TABLE 9. *Rate of polymerisation of methyl methacrylate compared with concentration of dibenzyl hyponitrite.*

Initiator concn. M (M)	$\sqrt{M}$	10^4R_p (mole l.$^{-1}$ sec.$^{-1}$)	$10^4R_p/\sqrt{M}$	Initiator concn. M (M)	$\sqrt{M}$	10^4R_p (mole l.$^{-1}$ sec.$^{-1}$)	$10^4R_p/\sqrt{M}$
0·01	0·1	1·76	17·6	0·0060	0·078	1·30	16·6
0·0089	0·094	1·59	17·0	0·0052	0·071	1·31	18·7
0·0075	0·086	1·51	17·5				

increased rapidly, though the kinetics were not strictly of the first-order. This may be due to the fact that dibenzyl hyponitrite has a small but finite absorption at 285·5 mμ ($\varepsilon = 20$). Half the final yield of benzaldehyde is formed in 2·75 hr. This compares with 2·46 hr. for the half-life of dibenzyl hyponitrite in cyclohexane at 35°. After several half-lives at 35° the yield of benzaldehyde remains constant (Table 8). The yield after 96 and 161 hr. at 35° is the same (49%), indicating that dibenzyl peroxide if present does not give benzaldehyde in this period of time. However, subjecting solutions which had undergone decomposition for 96 hr. at 35° to a further 65 hr. at 100° (at which the calculated half-life of dibenzyl peroxide is 55 hr.) increased the yield of benzaldehyde by 5%. The reverse of reaction (5) followed by disproportionation (4) is indicated. It appears that benzyloxy-radicals undergo disproportionation and dimerisation in a cage, and this is being further studied.

Polymerisation.—Both styrene and methyl methacrylate were polymerised by dibenzyl hyponitrite. Quantitative studies were made on the bulk polymerisation of methyl methacrylate, the rate being followed by the weight of polymer formed. The plot of percentage polymerisation against time gives a straight line passing through the origin, showing no inhibition period. The rate of polymerisation R_p is proportional to the square of the initiator concentration (Table 9). Further studies on this and other monomers are being undertaken.

EXPERIMENTAL

Materials.—Benzene and toluene. B.D.H. sulphur-free grades were stirred several times with concentrated sulphuric acid until the acid layer was only slightly coloured. The hydrocarbon layer was then separated from the acid and washed successively with water, 20% sodium carbonate solution, and water. Fractional distillation, after drying ($CaCl_2$), gave benzene, b. p. 80—80·5°, and toluene, b. p. 110—110·5°.

Chlorobenzene, bromobenzene, and p-*xylene.* B.D.H. reagents were dried ($CaCl_2$) and fractionally distilled: chlorobenzene, b. p. 132°; bromobenzene, b. p. 150°; *p*-xylene, b. p. 138°.

Nitrobenzene and o-*nitrotoluene.* "AnalaR" reagents (B.D.H.) were washed successively with 10% sodium hydrogen carbonate solution and water then dried ($MgSO_4$) and fractionally distilled: nitrobenzene, b. p. 210—211°; *o*-nitrotoluene, b. p. 220—221°. Freshly purified and distilled samples were used for kinetic studies, as aged samples give variable results.

Cyclohexane. Cyclohexane (B.D.H.) was shaken mechanically with 10% sulphuric acid and 1% oleum for 24 hr., then washed with water, 2N-sodium hydroxide solution, 10% potassium permanganate solution, and water. It was dried ($CaCl_2$) and fractionally distilled; b. p. 80·5°.

Carbon tetrachloride. "AnalaR" carbon tetrachloride, dried ($CaCl_2$) and fractionally distilled, had b. p. 76·5°.

Styrene and methyl methacrylate. The monomers (Light & Co.) were shaken thrice with 4% ice-cold sodium hydroxide solution and ice-water. After drying ($MgSO_4$) in a refrigerator they were fractionally distilled in a stream of argon immediately before use, giving styrene, b. p. 35°/10 mm., and methyl methacrylate, b. p. 100—101°.

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p-Benzoquinone. A B.D.H. sample was steam-distilled, dried, recrystallised from light petroleum (b. p. 80—100°), and dried over silica gel and paraffin wax; it had m. p. 115° (sublimes).

Chloranil. This was used as supplied by B.D.H.

Benzaldehyde. Crude benzaldehyde was shaken several times with cold 5% sodium carbonate solution. The benzaldehyde layer was then dried ($CaCl_2$) and distilled (b. p. 179—180°) in a current of argon immediately before use in spectroscopic analysis.

Benzyl alcohol. Benzyl alcohol was washed with sodium hydrogen sulphite solution and saturated brine. After being dried ($MgSO_4$) it was fractionally distilled in a stream of argon and used immediately for spectroscopic work, then having b. p. 204—205°.

Dibenzyl hyponitrite. The ester was prepared from silver hyponitrite and benzyl iodide according to Partington and Shah.[4] When freed from benzyl iodide by repeated precipitation from ether with light petroleum (b. p. 60—80°), it had m. p. 47—48° (decomp.). When heated rapidly the solid ester decomposed with a puff but not violently. The ester was stored in a desiccator kept in a refrigerator. Under these conditions deterioration is slow.

Products of Decomposition.—Solutions (0·5M) of freshly prepared dibenzyl hyponitrite in benzene and in cyclohexane were sealed under vacuum in vessels and allowed to decompose at 40°. After 5 days the ampoules were cooled and opened, and the solvent was removed under reduced pressure at room temperature in a stream of argon (to prevent oxidation of benzaldehyde). The residue was shaken in ether with a concentrated solution of sodium hydrogen sulphite. The addition compound was collected, washed with ether, and decomposed with sodium carbonate solution, and the liberated aldehyde was taken up in ether. The ether layer was then washed with sodium carbonate solution and evaporated in a stream of argon. The residue on treatment with 2,4-dinitrophenylhydrazine reagent gave large amounts of benzaldehyde 2,4-dinitrophenylhydrazone; after recrystallisation it had m. p. and mixed m. p. 235°. The dimedone had m. p. and mixed m. p. 198—200°. The ether solution which had been extracted with sodium hydrogen sulphite was dried and evaporated. The residue gave high yields of benzyl 3,5-dinitrobenzoate, m. p. and mixed m. p. 113°.

The highly dilute solutions left over from kinetic measurements gave tests for benzaldehyde only after storage, though after evaporation in the case of volatile solvents the odour of benzaldehyde was noticeable in the residual liquid which gave derivatives immediately.

Polymerisation Rates.—Equal volumes (5 ml.) of a solution of freshly prepared dibenzyl hyponitrite in freshly distilled methyl methacrylate were sealed in degassed ampoules. The ampoules were then simultaneously immersed in a thermostat (25°). At regular intervals the ampoules were removed from the bath and opened, and the contents completely transferred with the minimum quantity of benzene into methanol (100 ml.) containing quinol. The polymer was centrifuged off, washed with more methanol, and redissolved in the minimum amount of benzene at room temperature. After re-precipitation the polymer was collected on a sintered-glass crucible and dried *in vacuo* at 56° to constant weight.

Apparatus.—All thermostats were controlled to within 0·05°. Spectroscopic work was performed with an S.P. 500 Unicam spectrophotometer and fused-silica 1 cm. cells with ground-glass stoppers.

Vessels for manometric measurements were constructed from 1·5 cm. Pyrex tubing of varying lengths (depending on the volumes of nitrogen expected) up to 8 cm. and capacity 15 c.c. The bottom was sealed and rounded off, and there was attached to the top a standard-taper joint for connection to the vacuum-system. Magnetic stirring was provided. A capillary side-arm near the top of the vessel was fused to a vertical capillary tube 80 cm. long and of 0·05 mm. internal diameter, the bottom of which was immersed in a large pool of mercury. The vertical manometer tubing was mounted against a metre rule graduated in mm. The whole apparatus was of a single-fused construction and was tested for leaks before use. Careful cleaning with chromic acid and distilled water was followed by drying and degassing on a vacuum-line. Solutions were delivered into the main vessel through capillary tubes below the construction made to facilitate sealing-off between the main vessel and the standard-taper joint for attachment to the vacuum-system. After admission of the solution, the vessel was attached to the vacuum-system by the standard-taper joint and frozen in carbon dioxide–acetone. Evacuation then followed, through a tap which permitted communication to a vacuum-system (10^{-3} mm.). The tap was then closed and the solid allowed to thaw to dispel any entrapped gas. The cycle of freezing, evacuation, and thawing was repeated twice, the solution then frozen again, and

sealing carried out at the prepared constriction. After melting of the contents the main vessel was completely immersed in the appropriate thermostat. Pressure readings were taken at suitable intervals and corrected for the existing barometric pressure.

Agitation within the vessel was effected by a horse-shoe magnet (varnished to prevent rusting) mounted below the vessel on a shaft driven by a motor. Efficient agitation was necessary in order to avoid supersaturation and sudden jumps in pressure. In the case of very dilute solutions, when the volume of solution was large relative to the size of the vessel, stirring appeared to be insufficient and plots were slightly wavy.

Detection of Formaldehyde.—A 0·0456M-solution of dibenzyl hyponitrite in chlorobenzene (2·8 ml.) was sealed in a break-seal vessel under the same conditions as for the kinetic runs. The break-seal was then immersed in a thermostat at 40°, and after decomposition it was attached to the vacuum-system and the freshly evolved gases were transferred and absorbed in chromotropic acid. Analysis for formaldehyde was carried out according to the directions of Lee.[24] The absorption in the range 560—600 mμ was determined. No increase in absorption was found though 1 μmole of formaldehyde in the volume of solution used for analysis should show an optical density of 0·660 at 580 mμ.

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[24] Lee, *Analyt. Chem.*, 1956, **28**, 1621.

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348. *Nitramines and Nitramides. Part XII.* The Base-catalysed Decomposition of Some* ON*-Dialkylnitramines, and Evidence for the Existence of Geometrical Isomers.*

By ALEX. H. LAMBERTON and G. NEWTON.

The alkali-catalysed decomposition of R·N:NO·OR′ (R and R′ being alkyl groups) appears to proceed easily only when two α-hydrogen atoms are present, and an aldehyde can be formed by the reaction $-CH_2\cdot N{:}NO\cdot OR' \longrightarrow -CHO + N_2 + R'OH$. For R′ = Me, changing R from Me to Et or Pr^n slows the reaction by a factor of about 10; and, for R = Me, changing R′ from Me to Et or Pr^i brings about a slight increase in rate.

These observations apply only to the main bulk of the material prepared by treatment of the silver salt of $R\cdot NH\cdot NO_2$ with the halide R′X; in the majority of cases the behaviour of crude samples was consonant with the presence therein of up to 25% of a less stable geometrical isomer, which can be readily hydrolysed to the parent nitramine.

Purified samples gave rates of acid-catalysed decomposition in agreement with previous work: measurements in Parts IX and XI of this series are therefore not invalidated by the recognition of isomerism in the crude materials.

UMBGROVE and FRANCHIMONT [1,2] decomposed several *ON*-dialkylnitramines by heating them with aqueous potassium hydroxide, and Backer,[3] considering the reaction to be analogous to ester hydrolysis, was puzzled by the formation of nitrogen and an aldehyde

* Part XI, *J.*, 1957, 4198.

[1] Umbgrove and Franchimont, *Rec. Trav. chim.*, 1897, **16**, 359, 375.
[2] Umbgrove and Franchimont, *Rec. Trav. chim.*, 1898, **17**, 270.
[3] Backer, *Ahrens Sammlung*, 1912, **18**, 359.

in place of the expected primary nitramine. The fact that some primary nitramines are themselves decomposed by alkali [4] does not resolve the difficulty, since we have found that *ON*-dimethylnitramine was broken down, to liberate nitrogen, much more readily than the parent *N*-methylnitramine. The latter cannot, therefore, be an intermediate in the decomposition.

The early workers employed conditions (several hours at 100° in 12% aqueous potassium hydroxide) which were needlessly severe. We found that, at 70°, *O*-alkyl-*N*-methylnitramines were completely decomposed, in a few hours, by means of 0·1M-potassium hydroxide; but the *O*-methyl derivatives of ethyl- and n-propyl-nitramine were more stable by a factor of ten. The *O*-methyl derivatives of isopropyl- and t-butyl-nitramine yielded gas, but the rate of evolution was not significantly altered by changes in the concentration of alkali. Our results (obtained by the measurement of gas pressure at constant volume, with rigorously purified materials) are set out in Table 1.

Isomeric Forms of Dialkylnitramines.—The distinction between the *NN*- and *ON*-isomers was recognised [5] in 1894. Signs of a third, unstable, compound were found by Umbgrove and Franchimont,[2] who suggested the possibility of geometrical isomerism. In earlier papers of the present series [6] no sign of isomerism was found; for the materials, purified by repeated distillation *in vacuo*, were kinetically homogeneous on decomposition by means of aqueous acids. On extending this work to decomposition in alkaline solutions we found that crude samples (of most, but not all, of the *ON*-dialkylnitramines examined) did not give a kinetically homogeneous evolution of gas when warmed in aqueous potassium hydroxide. The initial gas evolution was comparatively rapid, and was accompanied by a fall in the concentration of potassium hydroxide. This behaviour was observed even after two or three distillations, though (at least for *O*-ethyl-*N*-methylnitramine) the impurity was to some extent concentrated in the higher-boiling fractions. The materials gave satisfactory elemental analyses; and the kinetic anomalies cannot be due to the *NN*-isomerides, which were shown (*a*) to be present only in very small quantities (<3%), and (*b*) to be relatively stable in alkaline solutions.

Removal of the Less-stable ON-*Dialkyl Isomeride.*—The crude materials could be purified by warming for a short time in aqueous alkali,* extraction with ether, and redistillation. After this treatment the decompositions yielded 95—99% of the theoretical quantity of gas, in place of the former 65—95%; and, as judged by the rate of evolution, were kinetically homogeneous. Further, there was now no rapid uptake of hydroxide ion; and the catalytic constants k_{OH^-} (Table 1) were in agreement with the slower, final, rates shown by the crude samples. One example may be given as an illustration. Crude *O*-ethyl-*N*-methylnitramine in 0·025M-potassium hydroxide at 70° gave an initial first-order rate of *ca.* $7{\cdot}2 \times 10^{-3}$ min.$^{-1}$; after 80 min. this had fallen to $4{\cdot}7 \times 10^{-3}$ min.$^{-1}$, and a separate experiment, with 0·0766M-alkali, suggested that at this stage the potassium hydroxide concentration had been reduced to about 0·015M, whence $k_{OH^-} \approx 0{\cdot}3$ l. mole^{-1} min.$^{-1}$ for the final stage of the run. After purification the decomposition was kinetically homogeneous, with $k_{OH^-} = 0{\cdot}37$ l. mole^{-1} min.$^{-1}$. The change in slope, for a first-order plot with the crude material, was thus largely due to a change in the concentration of potassium hydroxide. At faster rates (0·05 and 0·075M-KOH) the anomalous portion of the run was completed before the first observation of gas pressure. The (relative) change in alkali concentration was in these cases smaller; but an anomaly still remained, in that the linear plot, when extrapolated back to the time origin, gave an intercept of less than 100% of the total gas evolved.

Examination in Detail of the Decomposition of Crude O-*Ethyl*-N-*methylnitramine.*—

* Or, probably, by warming in distilled water alone, but this mode of purification has not been examined critically.

[4] Barrott, Gillibrand, and Lamberton, *J.*, 1951, 1282.
[5] Bamberger, *Ber.*, 1894, **27**, 359.
[6] Bruck and Lamberton, *J.*, 1955, 3997; 1957, 4198.

Control experiments showed that the abnormal course of gas evolution was not due to vapour-pressure effects exerted either by the initial nitramine, or by the products of decomposition. Nor was the slowing of the reaction an example of auto-retardation, since a closely similar reaction course was observed when fresh samples of the nitramine were decomposed in the spent solution from a previous run, or in a synthetic mixture containing, besides potassium hydroxide, the products of decomposition (formaldehyde and ethanol) in appropriate concentrations.

Measurements were made, in separate experiments, of (*a*) the course of gas evolution,

TABLE 1. *Decomposition of* ON-*dialkylnitramines, initially* 0·05M, *measured by gas evolution in aqueous potassium hydroxide at* 70°. (*First-order rate coefficients,* k_2 *in min.*$^{-1}$; *catalytic constants,* k_{OH^-},* *in l. mole*$^{-1}$ *min.*$^{-1}$.)

Run no.	Compound	Alkali (mole l.$^{-1}$ at 20°)	10^3k_2	k_{OH^-}	Run no.	Compound	Alkali (mole l.$^{-1}$ at 20°)	10^3k_2	k_{OH^-}
1	MeN:NO·OMe	0·105	24·0	0·23	12	EtN:NO·OMe	0·202	4·9	0·025
2	,,	0·0750	16·2	0·22	13	,,	0·150	3·6	0·025
3	,,	0·0488	11·1	0·23	14	,,	0·106	2·0$_5$	0·020
4	,,	0·0100	2·1	0·22	15	Pr^{n}N:NO·OMe	0·200	4·8	0·024
5	MeN:NO·OEt †	0·0754	25·6	0·35	16	,,	0·150	3·8	0·026
6	,,	0·0500	17·9	0·37	17	,,	0·100	2·3$_8$	0·024
7	,,	0·0250	9·0	0·37	18	Pr^{i}N:NO·OMe	0·211	0·2	
8	,,	0·0100	4·0	0·41	18	,,	0·025	0·4	
9	MeN:NO·OPr^i	0·0500	23·4	0·48	20	Bu^{t}N:NO·OMe	0·150 ‡	24·5	§
10	,,	0·0250	11·8	0·48	21	,,	0·100 ‡	29·0	
11	,,	0·0099	4·5	0·46	22	,,	0·050 ‡	25·1	

* Catalytic constants have been calculated on the assumption that the hydroxyl-ion concentration at 70° was 98% of that measured at room temperature.

† A plot of the catalytic constants for MeN:NO·OEt against [KOH] suggests a " water-rate " of $0·6 \times 10^{-3}$ min.$^{-1}$; but we think this erroneous, in view of the absence of any " water-rate " for the other *N*-methyl compounds.

‡ In H_2O–MeOH (75 : 25, v/v).

§ These rates show no relation to [KOH], but are in good agreement, after reasonable allowances for changes in temperature and solvents, with the " water-rates " previously [6] determined.

(*b*) the rise in formaldehyde concentration, and (*c*) the fall in concentration of potassium hydroxide. These measurements were repeated on the material purified by treatment with alkali, and are summarised in Table 5. It can be seen (lines A and B) that the evolution of gas, especially in the initial stages, was faster than the increase in the concentration of formaldehyde: this indicates either a separate source of gas, or (much less likely) the retention of formaldehyde in some intermediate product of decomposition. The removal of formaldehyde by the Cannizzaro reaction can only bear a minor responsibility, since the greater part of the " formaldehyde deficiency " (line C) was observed in the first 20 min., when the concentration of formaldehyde was small, and the rate of the Cannizzaro reaction would be reduced. The changes in " formaldehyde deficiency," after 40 min., are in reasonable agreement with our independent observations of the rate of the Cannizzaro reaction in comparable conditions of concentration and temperature. The concentration of potassium hydroxide (line D) also showed its most rapid fall at the commencement of the run, and the fall in potassium hydroxide concentration at any time was greater (compare lines D and E) than could have been accounted for if the " formaldehyde deficiency " had been due solely to the Cannizzaro reaction. The difference between lines D and E is approximately constant after 40 min.: this suggests that changes in the " formaldehyde deficiency " are then related stoicheiometrically to changes in [KOH], in terms of the relationship $2CH_2O \longrightarrow H{\cdot}CO_2H$.

The simplest and most likely explanation of the figures discussed in the preceding paragraph appears to be that the main reaction, yielding gas and formaldehyde, is accompanied by a more rapid reaction (or reactions) yielding gas and an acid, but no formaldehyde. This behaviour is consonant with the existence, in the crude material, of two

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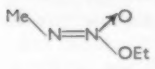
isomers of the structure MeN:NO·OEt, the major constituent being decomposed according to the reaction $MeN{:}NO{\cdot}OEt \xrightarrow{KOH} CH_2O + N_2 + EtOH$, and the minor constituent yielding in part gas ($MeN{:}NO{\cdot}OEt + H_2O \longrightarrow MeOH + N_2O + EtOH$?) and in part the stable nitramine salt by the reaction $MeN{:}NO{\cdot}OEt + KOH \longrightarrow MeN_2O_2K + EtOH$. Treatment with alkali of a crude (though neutral) sample of *O*-ethyl-*N*-methylnitramine has yielded methylnitramine, isolated as its cyclohexylamine salt.

Behaviour, in Comparison, of Purified O-*Ethyl*-N-*methylnitramine.*—These opinions are strongly supported by the results obtained from the purified material (Table 5, lines A′ to E′), when, effectively, the faster reactions had been allowed to run their course, and the residual (isomerically pure) nitramine recovered. In this case formaldehyde concentration is slightly ahead of gas evolution in the early stages—a not unexpected result, since the method of gas measurement tends to show a slight induction period on account of supersaturation. There is no early fall of significant size in the concentration of potassium hydroxide, and the " formaldehyde deficiency " which appears in the later stages is quantitatively related to the fall in alkali concentration: compare lines D′ and E′. Finally, the total yield of gas is now almost quantitative, in place of the 84% obtained from the impure sample. We felt confident, from these results, that we were now dealing with a homogeneous process of decomposition, strictly in accordance with the overall equation $MeN{:}NO{\cdot}OEt \longrightarrow CH_2O + N_2 + EtOH$, though followed by the Cannizzaro reaction $2CH_2O + KOH \longrightarrow H{\cdot}CO_2K + MeOH$; and it can be seen that [KOH] is not significantly altered before some 80% of the gas has been evolved.

Physical Properties of the Crude and Purified Samples, and Structure of the Isomers.—These properties support the hypothesis that the impure material contains a geometrical isomer of the more stable form. The ultraviolet spectrum of the purified material showed maximum absorption, in water, at a slightly shorter wavelength than for the crude sample; the infrared spectra, observed as smears, were almost precisely identical—with the exception of an absorption band at 1263 cm.$^{-1}$, found only in the crude sample. The refractive index was reduced by purification. The dipole moment of the crude sample was 2·6 D, reduced by purification to 1·8 D; bearing in mind the moments of the *cis*- and the *trans*-form of azoxybenzene (4·7 and 1·7 D, respectively), we think that our more stable isomeride probably has the *trans*-configuration (see inset).



General Survey of the ON-*Dialkylnitramines Prepared.*—Purification of the remaining materials (when required) always brought about a fall in the refractive index—a result consonant with the removal of a *cis*-isomer. The proportion of this less stable, presumed *cis*-, isomer in our crude preparations could be estimated by an extrapolation to the time origin of the final, and linear, portion of the first-order " log plot." The relative proportions of the isomerides so indicated cannot be precise, since any removal of alkali by the *cis*-isomer will have retarded the alkali-catalysed decomposition of the *trans*-isomer; but the figures are reasonable approximations. Our crude *O*-ethyl-*N*-methylnitramine contained 15—20% of the less stable isomer.

ON-Dimethylnitramine and *O*-methyl-*N*-t-butylnitramine appeared to be pure as first prepared; the volumes of gas evolved were normal, and there were no signs of kinetic inhomogeneity. The aldehyde products from *N*-ethyl-*O*-methylnitramine (crude: 30% of the less stable form) and *O*-methyl-*N*-propylnitramine (crude: 10% of the less stable form) could not be examined quantitatively, on account of the formation of coloured aldehyde resins; these (subsequent) reactions did not seem to give rise to any kinetic anomalies in runs with the purified materials. We have checked the nature of the gas evolved from an alkaline solution of crude *N*-ethyl-*O*-methylnitramine by means of infrared spectroscopic analysis: it was at least 99% nitrogen. Though the crude sample of *N*-isopropyl-*O*-methylnitramine showed an initial kinetic anomaly (corresponding to 20% of an alkali-unstable isomer), the purified material, and also *O*-methyl-*N*-t-butyl

nitramine, did not appear to undergo alkali-catalysed decomposition (see Table 1, and notes).

There remains *N*-methyl-*O*-isopropylnitramine (crude: 15—20% of the less stable form). Measurements of formaldehyde, of potassium hydroxide, and of gas evolution are reproduced in Table 6. It can be seen that for the crude sample, whilst the concentration of potassium hydroxide again shows an initial fall, there is no deficiency of formaldehye, in comparison with gas evolution in the early stages. The anomalies are removed by purification, and we conclude that the geometrical isomeride is in this case largely decomposed by the route $MeN{:}NO{\cdot}OPr^i + KOH \longrightarrow MeN{:}NO_2K + Pr^iOH$, without evolution of gas.

To conclude the discussion of isomerism we point out that the materials termed " crude" are so named for lack of a better term; all " crude " materials used for any measurements had been distilled at least twice, contained less than 3% of the *NN*-isomeride, and gave satisfactory analyses: and that we do not claim, in default of isolation of a pair of isomers, that our evidence as yet constitutes a full proof. The results in Tables 1—3 were all obtained from fully purified materials.

Activation Energies.—Some measurements have been made at temperatures other

TABLE 2. *The parameters A and E in the kinetic equation* $k = A \exp(-E/RT)$.

Run nos. and notes	Compound (initially (0·05M)	Values of k_{OH^-} (l. mole^{-1} min.$^{-1}$) measured by gas evolution at						$\log_{10} A$ (l. mole^{-1} sec.$^{-1}$)	E (kcal. mole^{-1})
		50°	51°	60°	70°	75°	80°		
a	MeN:NO·OMe				0·231	0·32$_5$	0·48	9	18
b	MeN:NO·OEt	0·050		0·123	0·34$_5$			11	21
c	MeN:NO·OPr^i		0·094	0·204	0·49			10	19
d	EtN:NO·OMe				0·0246	0·038	0·057	9	20
e	Pr^{n}N:NO·OMe				0·0262	0·044	0·066	11	22

Run nos. are grouped in order of increasing temperature, and concentrations of alkali are given in mole l.$^{-1}$ at 20°. (*a*) 0·0488M-KOH, 3, 23, 24: (*b*) 0·0754M-KOH, 25, 26, 5: (*c*) 0·0488M-KOH, 27, 28, 29: (*d*) 0·202M-KOH, 12, 30, 31: (*e*) 0·150M-KOH, 16, 32, 33. In view of the small number of determinations we do not feel it advisable to quote values of log A and E to a greater degree of precision.

TABLE 3. *Decomposition of* ON-*dialkylnitramines, initially* 0·05M, *measured by gas evolution in hydrochloric acid at* 45°. (*First-order rate coeff.* k_1 *in min.*$^{-1}$; *catalytic constant,* k_{H^+}, *in l. mole*$^{-1}$ *min.*$^{-1}$.)

Run no.	Compound	Acid (mole l.$^{-1}$ at 20°)	$10^3 k_1$	k_{H^+}	Average value of k_{H^+} from ref. 6
34	MeN:NO·OEt	0·50	19·5	0·039	0·044
35	,,	0·50	20·7	0·042	
36	MeN:NO·OPr^i	0·50	22·0	0·044	0·038, 0·044 *
37	EtN:NO·OMe	0·050	19·9	0·40	0·41
38	Pr^{n}N:NO·OMe	0·050	25·0	0·50	
39	,,	0·025	11·7	0·47	
40	Pr^{i}N:NO·OMe	0·0050	15·5	3·1	3·6
41	,,	0·0025 †	13·9	3·5	

* By ultraviolet measurements: attention had already been drawn [6] to the discrepancy between gas evolution and ultraviolet measurements for this compound, and it now appears that the ultraviolet values are the more accurate.

† Sulphuric acid; H^+ (calc.) at 45°, 0·0040M.

than 70°, and are reported in Table 2. The energies of activation are similar to those found [6] for decomposition by acids; but the frequency factors are somewhat smaller, and lie within the limits prescribed by Hinshelwood and Winkler [7] for bimolecular reactions.

Acid-catalysed Decomposition of Isomerically Pure ON-*Dialkylnitramines.*—Reasons could be suggested (but cannot now be proved) to account for the apparent homogeneity of the materials examined in earlier papers [6] of this series. We are pleased to find that

[7] Hinshelwood and Winkler, *J.*, 1936, 371.

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any errors in the previous values must be small, and do not in any way invalidate the conclusions drawn from the published figures. In Table 3 we give values of the catalytic constant K_{H^+} which have now been determined on isomerically pure materials. $Pr^nN{:}NO{\cdot}OMe$ had not been previously examined; the rate found fits normally into the series R = Me < Et < Pr^n < neo-C_5H_{11} < Pr^i ≪ Bu^t for R·N:NO·OMe.

Experimental

Reaction rates were evaluated on the basis of natural logarithms, and temperatures were controlled to within 0·1°. Concentrations of alkali or acid have been corrected on the assumption that the solutions showed the same expansion as water over the range 20—80°. The method of rate measurement by a manometric technique has been previously described:[8] we have found it advisable to lengthen (and support, by a rigid connection to the frame) the glass " tail " of the apparatus marked *F* in the Figure of ref. 8). This alteration ensures a positive internal pressure at the glass-to-rubber joint, and prevents the entry of air which forced us, occasionally, to discard otherwise satisfactory " runs."

Preparation and Purification of Materials.—All but one of the *ON*-dialkylnitramines have recently[6] been described. The silver salt of n-propylnitramine (47 g.) was refluxed for 6 hr. with methyl iodide (43 g.) in dry ether (400 ml.), and, after collection of the silver iodide, the filtrate was distilled to yield O-*methyl-N-n-propylnitramine* (probably containing some 10% of the *cis*-isomer), b. p. 71—73°/35 mm. (Found: N, 23·4. $C_4H_{10}N_2O_2$ requires N, 23·7%).

O-Ethyl-*N*-methylnitramine (19 g.) was purified by dissolution in water (850 ml.), addition of potassium hydroxide (50 ml. of 0·7M), and heating for 1 hr. at 70°. After cooling, the mixture was extracted with ether (4 × 200 ml.), and the extract was washed with water, dried (Na_2SO_4), and distilled to yield the residual isomerically pure nitramine of b. p. 40—42°/20 mm. With the exception of MeN:NO·OMe and $Bu^tN{:}NO{\cdot}OMe$, which appeared to be already pure by the test of kinetic homogeneity, all the *ON*-dialkylnitramines were similarly purified: physical properties are summarised in Table 4. The refractive indices were measured with an Abbé refractometer, and the dipole moment of *O*-ethyl-*N*-methylnitramine was determined by standard methods, benzene being used as a non-polar solvent.

Comparison of Gas Evolution, Formaldehyde Production, and Alkali Concentration.—The gas evolved (expressed as mmoles per l. of solution) was calculated from observations on the increase in pressure at constant volume, made in the rate-determination apparatus. For formaldehyde, aliquot parts (20 ml.) of a solution of the *ON*-dialkylnitramine in aqueous potassium hydroxide were kept at 70°, cooled rapidly, and treated with a solution (100 ml.)

Table 4. *Comparison of " crude " and " purified " samples of* ON-*dialkylnitramines.*

Compound		Analyses (%) Found C	H	N	Calc. C	H	N	n_D^{25}	U.V. Spectra in H_2O log $\varepsilon_{max.}$	mμ
MeN:NO·OMe		26·9	6·5	30·8	26·7	6·7	31·1		3·94	217
MeN:NO·OEt	Crude	34·9	7·8	27·0	34·6	7·7	26·9	1·4320	3·76	215
	Purified	34·8	7·8					1·4248	3·80	205
MeN:NO·OPr^i	Crude	40·3	8·2		40·6	8·5		1·4268	3·76	212
	Purified	40·3	8·6					1·4245	3·78	210 *
EtN:NO·OMe	Crude	34·8	7·5		34·6	7·7		1·4293	3·74	214
	Purified	34·8	7·7					1·4263	3·76	212
$Pr^nN{:}NO{\cdot}OMe$	Crude			23·4			23·7	1·4310	3·84	212
	Purified			23·9				1·4300	3·80	215
$Pr^iN{:}NO{\cdot}OMe$	Crude			24·0			23·7	1·4259	3·75	212
	Purified			23·5				1·4245	3·79	212 *
$Bu^tN{:}NO{\cdot}OMe$		45·9	9·2		45·5	9·1			3·74	215

* Independently determined[6] as, respectively, 3·81 at 213 and 3·70 at 213 mμ.

of 2,4-dinitrophenylhydrazine. After 24 hr. at 0°, the precipitate was collected, and dried at 100°. The reagent was prepared by warming 2,4-dinitrophenylhydrazine (10 g.) with hydrochloric acid (2 l. of 2N), filtering off excess of the hydrazine from the cooled solution, and saturating it with the formaldehyde hydrazone by addition of a little formaldehyde; then after 24 hr. at 0°, the suspension was allowed to warm to room temperature, and filtered before

[8] Barrott, Denton, and Lamberton, *J.*, 1953, 1998.

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use. Tests showed the precipitation to be >98% of quantitative, even in 0·05M-ethanol (ethanol of this concentration is formed by the complete decomposition of *O*-ethyl-*N*-methylnitramine). The potassium hydroxide concentration was measured by heating aliquot parts (5 ml.) of the nitramine solution, cooling rapidly, and titrating with hydrochloric acid. Our results are given in Tables 5 and 6.

TABLE 5. *Relation of gas evolution, formaldehyde production, and alkali concentration for the decomposition of* O-*ethyl*-N-*methylnitramine at* 70°.

All values in mmole $l.^{-1}$, as at 20°. Initial concentrations: lines A to E crude nitramine (50·5 mmoles $l.^{-1}$) in potassium hydroxide (76·6 mmoles $l.^{-1}$); lines A′ to E′, purified nitramine (50·0 mmoles $l.^{-1}$) in potassium hydroxide (75·0 mmoles $l.^{-1}$).

	Time (min.)	10	20	40	60	80	85	160	180
(A)	Gas evolved	15·5	21·8	29·8	34·3	37·7		42·3	
(B)	$[CH_2O]$		12·0	17·8	21·4	23·3		27·7	
(C) (= A − B)	Deficiency in $[CH_2O]$		9·8	12·0	12·9	14·4		14·6	
(D)	Fall in [KOH]		10·8	13·1	13·5	13·9		15·0	
(E) (= C/2)	Fall in [KOH] which could be due to Cannizzaro reaction		4·9	6·0	6·5	7·2		7·3	
(A′)	Gas evolved	11·4	19·9	31·6	38·4		43·2		49·0
(B′)	$[CH_2O]$	12·4	19·2	30·0	34·5		38·8		38·6
(C′) (= A′ − B′)	Deficiency in $[CH_2O]$	−1·0	0·7	1·6	3·9		4·4		10·4
(D′)	Fall in [KOH]	0·7	0·9	1·0	1·4		2·3		5·4
(E′) (= C′/2)	Fall in [KOH] which could be due to Cannizzaro reaction		0·4	0·8	2·0		2·2		5·2

TABLE 6. *Relation of gas evolution, formaldehyde production, and alkali concentration for the decomposition of* O-*isopropyl*-N-*methynitramine at* 70°.

All values in mmole $l.^{-1}$, as at 20°. Initial concentrations: lines A to E, crude nitramine (51·8 mmoles $l.^{-1}$) in potassium hydroxide (48·9 mmoles $l.^{-1}$); lines A′ to E′, purified nitramine (50·2 mmoles $l.^{-1}$) in potassium hydroxide (48·9 mmoles $l.^{-1}$).

	Time (min.)	10	30	60	120	240	300
(A)	Gas evolved	15·1	19·8	28·5	36·0	39·7	40·0
(B)	$[CH_2O]$	15·4	18·4	23·8	27·6	28·8	28·2
(C) (= A − B)	Deficiency in $[CH_2O]$	−0·3	1·4	4·7	8·4	10·9	11·8
(D)	Fall in [KOH]	3·6	5·6	6·2	8·3	10·0	9·9
(E) (= C/2)	Fall in [KOH] which could be due to Cannizzaro reaction		0·7	2·4	4·2	5·5	5·9
(A′)	Gas evolved	18·5	23·8	35·6	43·7	46·7	47·0
(B′)	$[CH_2O]$	17·6	22·3	31·0	36·5	34·7	34·7
(C′) (= A′ − B′)	Deficiency in $[CH_2O]$	0·9	1·5	4·6	7·2	12·0	12·2
(D′)	Fall in [KOH]	1·1	2·0	2·6	3·9	4·9	6·7
(E′) (= C′/2)	Fall in [KOH] which could be due to Cannizzaro reaction	0·5	0·8	2·3	3·6	6·0	6·1

Fractionation of O-*Ethyl*-N-*methylnitramine, and Hydrolysis of the Crude Material to yield Methylnitramine.*—An unpurified sample was distilled at 20 mm., and fractions were collected. Kinetic examination at 70° in 0·025M-potassium hydroxide gave the following observed first-order rates at, respectively, 20 and 80 min. from the start of the run: 10^3k ($min.^{-1}$) for initial material, 6·8 and 3·9; for fractions of b. p. 35—38°, 6·9 and 5·2; b. p. 38—42°, 6·2 and 5·1; b. p. 42—48°, 7·1 and 3·5. The highest-boiling fraction thus shows the greatest change in rate.

Another sample of *O*-ethyl-*N*-methylnitramine (5·4 g. of b. p. 42—46°/18—20 mm., n_D^{25} 1·4296) was redistilled at 20 mm. to yield the following fractions: (I) 1·5 g., b. p. <42°, n_D^{25} 1·4276; (II) 2·9 g., b. p. 42—44°, n_D^{25} 1·4301; (III) 0·3 g., b. p. >44°, n_D^{25} 1·4371. When 0·05M-solutions of the nitramine were heated in 0·083M-potassium hydroxide at 70°, the fall in alkali (moles per mole of total nitramine) was, respectively, for fractions (I), (II), and (III): 10 min., 0·10, 0·16, 0·36; 20 min., 0·13, 0·22, 0·50; 30 min., 0·16, 0·26, 0·58; and 40 min., 0·17, 0·28, 0·62. The n_D^{25} of fraction (II), when kept for 10 weeks, was found to have fallen

to 1·4262 (possibly through decomposition of the less stable isomer); and heating a 0·1M-solution to 70° in 0·136-potassium hydroxide led, in 30 min., to a loss of 0·20 mole of alkali per mole of nitramine.

Fraction (II) (825 mg., now of n_D^{25} 1·4262) was heated at 70° for 70 min. in potassium hydroxide (80 ml. of 0·136M). The cooled solution was washed with ether (4 × 20 ml.), and evaporated on the steam-bath to *ca.* 15 ml.; after re-cooling, it was acidified (13 ml. of 2N-hydrochloric acid) and extracted with ether (2 × 10, and 5 × 5 ml.). The extract was dried (Na_2SO_4), then basified by the addition of cyclohexylamine (0·1 ml.), to yield the crude salt (*ca.* 50 mg.); recrystallisation from ethanol–ether gave methylnitramine cyclohexylamine salt (25 mg.), m. p. and mixed m. p. 132° (Found: C, 47·8; H, 9·6. Calc. for $C_7H_{17}N_3O_3$: C, 48·0; H, 9·8%).

Concentration and Behaviour of the NN-*Isomers.*—Some of the *NN*-isomer is always produced on alkylation of the silver salts of primary nitramines, but is rapidly removed on fractionation. The residual concentration in our "crude" products (at least twice distilled) was determined by observation of the residual ultraviolet absorption after decomposition of the *ON*-isomers in 2N-hydrochloric acid at 45°; it was generally less than 1%, and never more than 3%. These small quantities of the *NN*-isomers could not cause the anomalies which have been discussed. In addition, for comparison, we prepared *N*-ethyl-*N*-methylnitramine by the alkylation of ethylnitramine with methyl iodide and potassium hydroxide in ethanol, and removed any *ON*-isomers by shaking with 20% sulphuric acid for 1 hr. at room temperature, followed by redistillation; the product had b. p. 100—102°/30 mm. (Found: C, 34·7; H, 7·8. Calc. for $C_3H_8N_2O_2$: C, 34·6; H, 7·7%). Heating this (0·05M) with potassium hydroxide (0·0115M) at 70° had little effect on the alkali concentration, the observed fall (on titration with hydrochloric acid) in moles per mole of nitramine being: in 40 min., 0·006; 80 min., 0·004; 120 min., 0·006; 300 min., 0·008; and 1440 min., 0·020. We have also attempted to follow the decomposition of *NN*-dimethylnitramine by colorimetric determination of the nitrite produced, and by using more drastic conditions (2·07M-potassium hydroxide at 90°) to obtain a measurable rate. No gas was evolved, and only some 50—60% of the expected nitrite was obtained. It seems that the traditional equation $CH_3{\cdot}N(NO_2){\cdot}CH_3 + KOH \longrightarrow CH_2O + KNO_2 + CH_3{\cdot}NH_2$ does not provide a full picture of the decomposition, and that *NN*-dimethylnitramine is much more stable towards alkali than is the *ON*-isomer.

Behaviour of O-*Ethyl*-N-*methylnitramine on being heated in Water.*—A solution (0·05M) of the crude nitramine in distilled water at 70° rapidly evolved gas; evolution ceased after about 0·5 hr., when some 0·2 mole had been evolved per mole of total nitramine. The purified material was relatively stable, giving no gas on similar treatment.

Analysis of the Observed Course of Decomposition for the Unpurified ON-*Dialkylnitramines.*—Frost and Pearson [9] discuss the resolution of two parallel first-order reactions producing a common product. If $A \xrightarrow{k_1} C$, $B \xrightarrow{k_2} C$, and C is measured, then—if k_1 is considerably greater than k_2—the value of k_2 can be determined from the latter portion of the logarithmic plot of $(C_\infty - C)$ against time, when the reaction $A \longrightarrow C$ is effectively complete. Extrapolation back to the time origin of the line used to determine k_2 gives values of B, and hence of A $(=C_\infty - C - B)$. If our samples contained only two isomers, both of which showed first-order (or pseudo-first-order) decomposition to yield one mole of gas per mole of nitramine, then the analysis would fit, it being irrelevant, kinetically, whether the gas measured was nitrogen or nitrous oxide.

Unfortunately, part at least of A gives an acid, but no gas; and the acid reduces the rate of gas evolution from B by neutralisation of the potassium hydroxide. The analysis cannot, therefore, be precise; but good first-order log plots were obtained in three cases out of the four examined: the exception being *O*-isopropyl-*N*-methylnitramine, where there is reason to think that the unstable isomer was converted almost wholly into the acid, methylnitramine. Though we do not consider the numerical values of k_1 to be significant, the linear plots show that the observed kinetic anomalies were not due to factors of a random character.

Infrared Spectra of the ON-*Dialkylnitramines.*—Smears of the liquids were examined, for wavelengths 2—15 μ, a Grubb–Parsons double-beam spectrometer being used. They showed strong absorption at 1554 ± 10 and 1242 ± 10 cm.$^{-1}$. In several cases the band at 1554 cm.$^{-1}$ was flat-topped, and may represent more than one absorption frequency: it corresponds closely

[9] Frost and Pearson, "Kinetics and Mechanism," Wiley, New York, 1953, p. 149.

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to the *as*-stretching vibration in alkyl nitroparaffins [10] and is within the range suggested by Bellamy [11] for the same vibration in *N*-nitro-compounds. If the second absorption corresponds to the *s*-stretching vibration of the nitro-group, it has been displaced further than had been previously suggested [11] (*viz.*, C–NO_2 *ca.* 1380—1340 cm.$^{-1}$; N–NO_2, *ca.* 1300—1250 cm.$^{-1}$). In interpretation it should be remembered that the *ON*-dialkyl compounds do not have a free, terminal nitro-group; and that the nitramines considered by Bellamy are possibly not typical of the simple alkyl compounds.

All our *ON*-dialkyl compounds showed a medium-to-weak absorption band at 702 ± 5 cm.$^{-1}$, though in one case (MeN:NO·OPr^i) this was largely concealed by a more general absorption. The spectra of the " crude " and the " purified " materials were almost identical. The major absorption peaks between 2000 and 1000 cm.$^{-1}$ were as follows: MeN:NO·OMe, 1559, 1381, 1245, 1040; MeN:NO·OEt, 1562, 1444, 1381, 1242, 1032; MeN:NO·OPr^i, 1545, 1378, 1243, 1102, 1022; EtN:NO·OMe, 1562, 1460, 1434, 1338, 1240, 1000; Pr^{n}N:NO·OMe, 1562, 1463, 1429, 1338, 1239, 1013; Pr^{i}N:NO·OMe, 1548, 1465, 1331, 1239, 1009; and Bu^{t}N:NO·OMe, 1559, 1460, 1251, 1234, 1009.

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[10] Brown, *J. Amer. Chem. Soc.*, 1955, **77**, 6341.
[11] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, Chapter 17.

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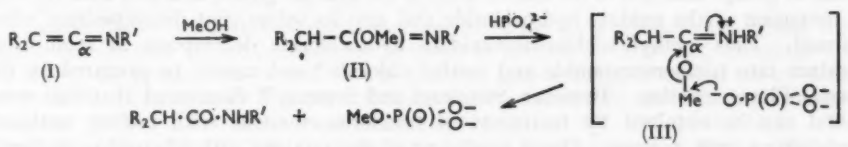
349. *The Reaction between Acetimidates and Acid Esters of Phosphoric Acid.*

By R. J. W. CREMLYN.

Methyl *N*-methyldi(methylsulphonyl)acetimidate and methyl trichloroacetimidate react with secondary phosphates to yield the corresponding tertiary phosphates; but ethyl *N*-methyldi(methylsulphonyl)acetimidate and methyl diphenyl-*N*-*p*-tolylacetimidate do not produce tertiary phosphates under comparable conditions.

KHORANA [1] prepared a number of mixed tertiary phosphates by the action of mono- and di-esters of phosphoric acid on *O*-alkylisoureas. The latter were obtained by reaction of alcohols with diarylcarbodi-imides in the presence of the corresponding alkoxide. Dialkylcarbodi-imides were unreactive, presumably owing to the relatively high electron density at their central carbon atom, which would be the initial point of attack by alkoxide ions (cf. Hünig *et al.*[2]). By analogy, alkyl acetimidates could be useful in syntheses of tertiary



phosphates. Diphenylketen *p*-tolylimide (I; R = Ph; R' = C_6H_4Me) [3] and di(methylsulphonyl)keten methylimide (I; R = SO_2Me, R' = Me) [4] react with methanol to give high yields of the corresponding methyl acetimidates (II); the former requires the presence

[1] Khorana, *Canad. J. Chem.*, 1954, **32**, 227.
[2] Hünig, Lehmann, and Grimmer, *Annalen*, 1953, **579**, 77.
[3] Stevens and French, *J. Amer. Chem. Soc.*, 1953, **75**, 657.
[4] Backer and Dijkstra, *Rec. Trav. chim.*, 1954, **73**, 575, 695.

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of sodium methoxide, but the latter will react with boiling methanol alone. Di(methylsulphonyl)keten methylimide should react more readily with alcohols than does diphenylketen *p*-tolylimide, since the two strongly electrophilic methylsulphonyl groups will increase the formal positive charge on the central carbon atom (C_α) more readily than the weakly electron-withdrawing phenyl groups. Methyl *N*-methyldi(methylsulphonyl)-acetimidate (II; R = SO_2Me, R′ = Me) has been treated with phosphates under various conditions. With an equimolar quantity of dibenzyl hydrogen phosphate, the optimum preparative conditions (heating in nitromethane solution at 90—110°) gave a 71% yield of dibenzyl methyl phosphate. Use of dioxan, boiling benzene, boiling aqueous acetone, or dimethylformamide at 90—100°, afforded yields of 62, 40, 6, and 6%, respectively. Substitution of dibenzyl tetramethylammonium phosphate for the free acid reduced the yield of dibenzyl methyl phosphate to 53%, but use of diphenyl hydrogen phosphate had little effect on yield. However, when phenyl dihydrogen phosphate (0·5 mole) in dioxan was substituted, the yield of dimethyl phenyl phosphate was only 25%. Ethyl *N*-methyldi(methylsulphonyl)acetimidate was similarly prepared, though the yield was only 46%; but subsequent treatment with phosphates in nitromethane and other solvents failed to produce tertiary phosphates. Numerous unsuccessful attempts have been made to prepare other alkyl *N*-methyldi(methylsulphonyl)acetimidates by reaction of the keten imide with the appropriate alcohol. Methyl diphenyl-*N*-*p*-tolylacetimidate (II; R = Ph, R′ = C_6H_4Me) was treated with dibenzyl or diphenyl hydrogen phosphate in hot nitromethane and dioxan, but the phosphate was largely recovered unchanged. The inertness of methyl diphenyl-*N*-*p*-tolylacetimidate is probably explained by the strong electromeric effect of the *p*-tolyl group neutralising the positive charge on the protonated nitrogen atom, and therefore preventing appreciable removal of electrons from the central carbon atom (C_α) upon which the success of the phosphorylation ultimately depends (cf. III).

A general method for the preparation of imidate hydrochlorides (IV; X = Cl) is treatment of a nitrile with an alcohol in the presence of dry hydrogen chloride.[5] These compounds, when heated in various solvents, decompose into the amide and the alkyl chloride,[6] the rate of decomposition being dependent on the solvent and the nature of the anion.[7] In chloroform and t-butyl alcohol pyrolysis proceeds by the S_N2 mechanism:[8]

This suggested that pyrolysis of alkyl acetimidate phosphates (IV; X = $H_2PO_4^-$) might afford a useful synthesis of mixed tertiary phosphates. The presence of electrophilic atoms or groups attached to the carbon atom of the cyanide group, increases both the ease of formation of the imidate hydrochloride and also its subsequent decomposition when warmed. Thus methyl trichloroacetimidate hydrochloride decomposes at room temperature into trichloroacetamide and methyl chloride [9] and cannot be prepared by the normal Pinner reaction. However, Steinkopf and Semmig [10] discovered that this compound can be obtained by treatment of trichloroacetonitrile with boiling methanol containing a little acetone. Direct treatment of this mixture with dibenzyl or diphenyl hydrogen phosphate in hot nitromethane gave the corresponding methyl tertiary phosphates in approximately 45% yield. Unsuccessful attempts were made to obtain other

[5] Pinner, *Ber.*, 1883, **16**, 352, 1643 *et seq.*
[6] Lengfeld and Stieglitz, *Amer. Chem. J.*, 1894, **16**, 70; Stieglitz, *ibid.*, 1899, **21**, 101.
[7] McElvain and Tate, *J. Amer. Chem. Soc.*, 1951, **73**, 2233.
[8] Stevens, Morrow, and Lawson, *J. Amer. Chem. Soc.*, 1955, **77**, 2341.
[9] Steinkopf, *Ber.*, 1907, **40**, 1643.
[10] Steinkopf and Semmig, *Ber.* 1920 **53**, 1149.

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trichloroacetimidates from the appropriate alcohol and trichloroacetonitrile. Recently, however, several of these imidates have been prepared by Cramer,[11] who showed that reaction could be promoted by the presence of weakly alkaline catalysts; and their subsequent phosphorolysis in boiling acetonitrile solution gave the corresponding mixed tertiary phosphates in 30—90% yield.[12]

Experimental

*Methyl Diphenyl-*N*-p-tolylacetimidate.*—Diphenylketen *p*-tolylimide (0·297 g.) in dry ether (3 c.c.) was treated with boiling methanol (6 c.c.) and sodium methoxide (0·035 g.), as described by Stevens and French.[3] The methyl ester formed needles (0·285 g.; m. p. 95—97°) on recrystallisation from light petroleum (b. p. 60—80°)–chloroform.

The corresponding *ethyl ester* was prepared similarly; it recrystallised from ethanol as prisms, m. p. 103—105° (73%) (Found: C, 83·7; H, 7·1; N, 4·5. $C_{23}H_{23}NO$ requires C, 83·9; H, 7·0; N, 4·3%).

Methyl N*-Methyldi(methylsulphonyl)acetimidate.*—Di(methylsulphonyl)keten *N*-methylimide (0·211 g.) was boiled under reflux with excess of methanol (15 c.c.) for 3 hr. Removal of the methanol and recrystallisation from benzene–chloroform afforded the methyl ester (211 mg.), m. p. 137—140° (lit.,[3] m. p. 143—144°) (Found: C, 29·6; H, 5·2; N, 6·0. Calc. for $C_6H_{13}NO_6S_2$: C, 29·6; H, 5·3; N, 5·8%).

The *ethyl ester*, similarly prepared, crystallised from light petroleum (b. p. 60—80°)–chloroform in prisms, m. p. 104—106° (46%) (Found: C, 32·5; H, 6·0; N, 5·7. $C_7H_{15}NO_6S_2$ requires C, 32·7; H, 5·8; N, 5·5%).

Dibenzyl Methyl Phosphate.—Methyl *N*-methyldi(methylsulphonyl)acetimidate (0·243 g., 1 mmole) was heated at 90—110° with dibenzyl hydrogen phosphate (0·278 g., 1 mmole) in nitromethane (10 c.c.) for 36 hr. The solution was evaporated under reduced pressure (bath temp. 30—40°), cooled, and shaken with anhydrous benzene (10 c.c.); *N*-methyldi(methylsulphonyl)acetamide, m. p. 210—212° (0·192 g., 84%), was deposited. The filtrate was diluted with benzene (50 c.c.), and washed successively with 50% aqueous sodium hydrogen carbonate, water, 1N-hydrochloric acid, and water, dried (anhydrous sodium sulphate), and evaporated under reduced pressure. The resulting dibenzyl methyl phosphate was a pale yellow oil (0·206 g., 71%), n_D^{21} 1·5342 (Found: C, 61·5; H, 6·0. Calc. for $C_{15}H_{17}O_4P$: C, 61·6; H, 5·8%).

Methyl Diphenyl Phosphate.—Similarly prepared, but by use of diphenyl hydrogen phosphate, this ester [13] was obtained as an oil (0·179 g., 68%), n_D^{21} 1·5320 (Found: C, 58·9; H, 5·2. Calc. for $C_{13}H_{13}O_4P$: C, 59·1; H, 4·9%).

Dimethyl Phenyl Phosphate.—Methyl *N*-methyldi(methylsulphonyl)acetimidate (0·080 g., 0·33 mmole) was heated at 80° with phenyl dihydrogen phosphate (0·030 g., 0·17 mmole) in dioxan (10 c.c.) for 40 hr. After concentration under reduced pressure, cooling, and addition of benzene (5 c.c.), *N*-methyldi(methylsulphonyl)acetamide (0·074 g., 82%), m. p. 210—212° separated. The liquor gave a pale yellow oil (0·023 g.; 25%) shown to be dimethyl phenyl phosphate, by treatment with calcium iodide in boiling ethyl methyl ketone.[13] This afforded calcium methyl phenyl phosphate (0·020 g.), m. p. >300° (Found: C, 39·8; H, 3·9; P, 14·7. Calc. for $C_{14}H_{16}O_8P_2Ca$: C, 40·4; H, 3·9; P, 14·9%).

Dibenzyl Methyl Phosphate.—Trichloroacetonitrile (0·435 g., 3 mmoles) was boiled with anhydrous methanol (10 c.c.) containing 10 drops of acetone for 8 hr. (cf. Steinkopf and Semmig [10]); the pungent odour of the nitrile had then largely disappeared, and the methanol was removed under reduced pressure. The residual oil was heated with dibenzyl hydrogen phosphate (0·834 g., 3 mmoles) in nitromethane (10 c.c.) at 90—100° during 48 hr. The solvent was removed under reduced pressure, and the product dissolved in benzene (200 c.c.) and washed successively with 2N-hydrochloric acid, water, aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and evaporated. The oil (0·476 g.), on treatment with calcium iodide in boiling ethyl methyl ketone,[13] furnished a white solid (0·168 g.), m. p. >300°. Paper chromatography (n-butanol–water, 86 : 14) revealed two phosphorus-containing spots (R_F values 0·40, 0·80), identical with those obtained from authentic dibenzyl methyl phosphate

[11] Cramer, Pawelzik, and Baldauf, *Ber.*, 1958, **91**, 1049.
[12] Cramer, Pawelzik, and Lichtenthaler, *Ber.*, 1958, **91**, 1555.
[13] Cremlyn, Kenner, Mather, and Todd, *J.*, 1958, 528.

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under similar conditions. The weight of mixed calcium salts indicated a 50% yield of this phosphate.

Methyl Diphenyl Phosphate.—Methyl trichloroacetimidate, prepared *in situ* as above, gave on treatment with one mole of diphenyl hydrogen phosphate in nitromethane under similar conditions, an estimated 40% yield of methyl diphenyl phosphate.

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350. *Synthesis of Quinol Monophosphates from Vitamin K_1, Ubiquinone, and Other Quinones, and Experiments on Oxidative Phosphorylation.*

By K. J. M. ANDREWS.

A number of quinol mono(dibenzyl phosphates) have been synthesised by the action of dibenzyl phosphite on quinones. Hydrogenolysis of these phosphates readily gave the required acid esters. Similarly, from benzyl ethyl phosphite, ethyl hydrogen phosphates were prepared.

Data are presented for the dephosphorylation of quinol monophosphates, in the presence of oxygen, and examples of oxidative phosphorylation are given.

THERE is evidence that naphthaquinone derivatives [1,2] and ubiquinone [3,4] are involved in oxidative phosphorylation in animal tissues, possibly as the phosphates. It has been suggested that the high-energy phosphate bond might first be formed with the quinols, and some theoretical and experimental evidence favours the formation of a quinol monophosphate or semiquinone phosphate.[5-7] These quinol phosphates have the additional value of being presumably water-soluble. It was therefore of interest to prepare quinol monophosphates, particularly dihydrovitamin K_1 and ubiquinol monophosphates.

One method of preparing quinol monophosphates is the phosphorylation of the monoacyl derivatives followed by deacylation.[8,9] However, the monoesters are often difficult or impossible of access and the deacylation involves concomitant dephosphorylation. It has been shown that dialkyl phosphites react with quinones to give the quinol mono(dialkyl phosphates),[10-12] and the reaction of menaphthone with diethyl phosphite produces the two possible monophosphates.[12] It was therefore thought that, by using suitably substituted phosphites, the substituents could be removed from the phosphate to give the required dihydrogen phosphate. Dibenzyl phosphite, in benzene or acetonitrile with a metal alkoxide as catalyst, reacted readily with a variety of quinones, to give the dibenzyl phosphates. Benzoquinone, for example, reacted vigorously with dibenzyl phosphite, under the standard conditions. The colourless product was a phosphate, and not a

[1] Martius, *Biochem. Z.*, 1956, **327**, 407.
[2] Anderson and Dallam, *J. Biol. Chem.*, 1959, **234**, 409.
[3] Hatefi and Quiros-Perez, *Biochim. Biophys. Acta*, 1959, **31**, 502.
[4] Pumphrey and Redfearn, *Biochem J.*, 1959, **73**, 3P.
[5] Clark, Kirby, and Todd, *Nature*, 1958, **181**, 1650.
[6] Harrison, *Nature*, 1958, **181**, 1131.
[7] Wieland and Pattermann, *Angew. Chem.*, 1958, **70**, 313.
[8] Hirschmann, U.S.P. 2,913,477.
[9] Wieland and Pattermann, *Chem. Ber.*, 1959, **92**, 2917.
[10] Diefenbach, G.P. 937,956.
[11] Ramirez and Dershowitz, *J. Org. Chem.*, 1957, **22**, 1282.
[12] Andrews and Atherton, *J.*, 1960, 4682.

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phosphonate, since it did not contain a carbonyl group and gave a monotoluene-*p*-sulphonate the infrared spectrum of which showed no hydroxyl band. Whereas no heating was required with alkylated quinones, reaction with chloranil and 2-chloro-3-methyl-1,4-naphthaquinone was sluggish and heat was necessary. High yields were obtained with the symmetrical alkylated quinones but the unsymmetrical ones gave mixtures and losses were considerable in the fractional crystallisations.

Mono(benzyl ethyl phosphates), prepared from a number of quinones and benzyl ethyl phosphite, were readily converted into the ethyl hydrogen phosphates by hydrogenolysis.

Acylation of the phosphates, either at the dibenzyl or the dihydrogen phosphate stage, gave a series of acyl phosphates.

2-Methyl-1,4-naphthaquinone and dibenzyl phosphite gave a mixture which was separated into two colourless crystalline compounds, m. p. 118—119° and 85—86·5°. These were phosphates, since they both formed non-hydroxylic monobenzoates. From the investigation of the monobenzoates it was concluded that the compound of m. p. 118—119° was 2-methyl-1,4-naphthaquinol 4-(dibenzyl phosphate) and that of m. p. 85—86·5° was the 1-(dibenzyl phosphate).

Hydrogenolysis of 2-methyl-1,4-naphthaquinol 1- and 4-(dibenzyl phosphate) readily gave the dihydrogen phosphates. These were acetylated and converted into the anilinium salts. 2-Methyl-1,4-naphthaquinol 1-acetate 4-(anilinium hydrogen phosphate) was also prepared by phosphorylation of 2-methyl-1,4-naphthaquinol 1-acetate with dibenzyl phosphorochloridate followed by hydrogenation and addition of aniline. 2-Methyl-1,4-naphthaquinol 1-acetate 4-(anilinium hydrogen phosphate) from the phosphite reaction was identical with that from this unambiguous synthesis.

It had been noted [12] that the temperature of the reaction affected the yield of dialkyl phosphates. It has now been found that the solvent has an effect: *e.g.*, in the reaction of dibenzyl phosphite with menaphthone in acetonitrile in presence of potassium t-butoxide at $<40°$, the ratio of 1- to 4-(dibenzyl phosphate) was 4 : 1 whereas, in benzene it was 1·25 : 1.

Vitamin K_1 reacted very similarly to the simple quinones, *i.e.*, the reaction mixture became warm and the orange-yellow colour was practically all discharged. Hydrogenolysis of the oily mono(dibenzyl phosphate) obtained gave the required dihydrovitamin K_1 monophosphate. Benzoylation of the dibenzyl phosphate and, after hydrogenolysis, addition of aniline to the phosphoric acid ester gave a colourless crystalline anilinium salt which was not identical with authentic dihydrovitamin K_1 1-benzoate 4-(anilinium hydrogen phosphate): analytical data and its infrared spectrum showed it to be a phosphate and, therefore, it was concluded that predominantly the 1-phosphate had been formed by the phosphite reaction. Acetylation and propionylation at the dibenzyl phosphate stage enabled the 4-acyl ester 1-phosphates to be prepared. By again using benzyl ethyl phosphite, it was possible to prepare the dihydrovitamin K_1 1-(benzyl ethyl phosphate) and thus the ethyl hydrogen phosphate. Phosphorylation of the benzyl ethyl phosphate with phosphorus oxychloride, followed by hydrogenation, readily gave the dihydrovitamin K_1 1-(ethyl hydrogen phosphate) 4-(dihydrogen phosphate).

Ubiquinone$_{(50)}$ also formed a faintly yellow dibenzyl phosphate in the same way, and hydrogenolysis of this, with Lindlar catalyst in order that the side chain should not be hydrogenated, gave the colourless dihydrogen phosphate.

Similarly the monophosphates were obtained from vitamin $K_{2(10)}$ and α-tocopherol quinone. The position of the phosphate group was not proved in these compounds but, by analogy with vitamin K_1, the product was probably mainly the 1-phosphate.

In aqueous solution the monophosphates, particularly the naphthaquinol monophosphates, were relatively unstable in an oxygen atmosphere (see Table 4), in accordance with the oxidative dephosphorylation mechanism described by Clark, Kirby, and Todd.[5] In a Warburg experiment with 2,3-dimethylnaphthaquinol 1-phosphate in buffered solution (pH 6·9) at 37°, there was negligible absorption under oxygen, and at pH 8·3 there

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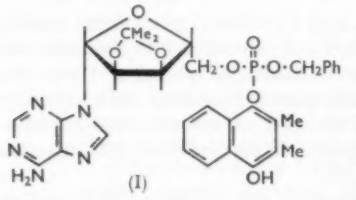
was a slow absorption for 20 min., then a rapid linear absorption for 55 min., by which time the theoretical volume of oxygen for the formation of quinone and orthophosphate had been used. There was also a further slow but small uptake. The extra volume of oxygen required is probably due to the oxidation of the quinone liberated. It was shown that when the theoretical volume of oxygen had been absorbed the liberation of orthophosphate was 80%. At pH 10·5 the uptake was too rapid for satisfactory measurement.

Clark, Kirby, and Todd,[5] and Wieland and Pattermann,[7,9] observed that quinol monophosphates act as phosphorylating agents in the presence of oxidising agents. Similarly, we found that 2,3-dimethylnaphthaquinol monophosphate or dihydrovitamin K_1 monophosphate, when shaken with triethylamine, charcoal, and anhydrous copper sulphate in ethanol under oxygen at 60°, gave the quinone and ethyl phosphate. With dihydrovitamin K_1 monophosphate there was also paper-chromatographic evidence for the formation of a pyrophosphate.

Benzyl phosphites of a variety of complex hydroxy-compounds can be prepared by using the *O*-benzylphosphorous–*OO*-diphenylphosphoric anhydride reagent.[13] Therefore, it was of interest to see if the quinone reaction would readily lead to the phosphate, particularly since the usual procedure (formation of the phosphorochloridate followed by hydrolysis [13,14]) often gives low yields. 2′,3′-Isopropylidineadenosine benzyl phosphite [13] with 2,3-dimethyl-1,4-naphthaquinone readily gave the phosphate (I); anionic fission of the benzyl group, followed by aerial oxidation of an alkaline aqueous solution of the hydrogen phosphate gave the quinone and 2′,3′-isopropylideneadenylic acid. The synthesis of adenylic acid, in low yield, was completed by hydrolysis of the isopropylidene group.



(I)

Experimental

" System A " refers to paper chromatography on Whatman 3MM paper (previously treated with a 5% solution of silicone fluid in light petroleum and dried) with acetic acid–water–propan-2-ol (2·5 : 37·5 : 60 v/v) at room temperature. For " system B " Whatman no. 1 paper and butan-1-ol–acetic acid–water (5 : 2 : 3) were used.

2-Methyl-1,4-naphthaquinol 1-(Dibenzyl Phosphate) and 4-(Dibenzyl Phosphate).—2-Methyl-1,4-naphthaquinone (17 g.) was stirred with dibenzyl phosphite (31·4 g.) in dry benzene (150 ml.) while N-potassium t-butoxide in t-butyl alcohol–benzene (1 ml.) was added slowly at <40°. After cooling was no longer necessary, the mixture was stirred at room temperature for a further hour, then filtered, washed with water, dried, and evaporated. An oil remained which readily crystallised on addition of carbon tetrachloride followed by cyclohexane. Colourless needles (31 g.; m. p. 109—113°) were obtained that partly dissolved in ether. The insoluble part, recrystallised from ethanol, gave needles (9·7 g.) of the *4-phosphate*, m. p. 118—119° (Found, in material dried *in vacuo* at 60°: C, 69·5; H, 5·1; P, 7·3. $C_{35}H_{33}O_5P$ requires C, 69·1; H, 5·3; P, 7·1%). Addition of light petroleum (b. p. 40—60°) to the solution of the other part in ether gave the *1-(dibenzyl phosphate)* (12·2 g.), m. p. 80—81°. Three recrystallisations from ethyl acetate–light petroleum (b. p. 40—60°) raised the m. p. to 85—86·5° (Found, in material dried *in vacuo* at 40°: C, 69·4; H, 5·1; P, 6·9%).

Reaction in acetonitrile gave 36 g. of crude product which was separated into 20·2 g. of m. p. 81—83° and 4 g. of m. p. 115—119°.

2-Methyl-1,4-naphthaquinol 4-Benzoate 1-(Dibenzyl Phosphate).—2-Methyl-1,4-naphthaquinol 1-(dibenzyl phosphate) (1·1 g.) was treated in pyridine at room temperature with benzoyl chloride during 2 hr. The *benzoate* (1·06 g.), recrystallised twice by dissolution in hot ether (a little ethyl acetate was added in the second recrystallisation) and addition of light petroleum

[13] Corby, Kenner, and Todd, *J.*, 1952, 3669.
[14] Kenner, Todd, and Weymouth, *J.*, 1952, 3675.

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(b. p. 40—60°), gave colourless prisms, m. p. 93—94° (Found, in material dried *in vacuo* at 50°: C, 71·0; H, 5·1; P, 5·7. $C_{32}H_{27}O_6P$ requires C, 71·4; H, 5·1; P, 5·8%).

2-Methyl-1,4-naphthaquinol 1-Benzoate 4-(Dibenzyl Phosphate).—(A) 2-Methyl-1,4-naphthaquinol 4-(dibenzyl phosphate) (1·1 g.) was benzoylated and recrystallised twice as above. The crude product (1·3 g.) had m. p. 80—82° and the recrystallisations gave plates (800 mg.), m. p. 85—86°. There was no m. p. depression on admixture with *2-methyl-1,4-naphthaquinol 4-benzoate 1-(dibenzylphosphate)* prepared as below and the infrared spectra were identical (Found, in material dried *in vacuo* at 50°: C, 71·6; H, 4·8; P, 5·6. $C_{32}H_{27}O_6P$ requires C, 71·4; H, 5·1; P, 5·8%).

(B) 2-Methyl-1,4-naphthaquinol 1-benzoate [15] (0·7 g.) was suspended in a solution of dibenzyl phosphite (0·7 g.) in dry carbon tetrachloride (5 ml.) and triethylamine (0·5 ml.) was added. The mixture was shaken; it became warm, the solid dissolved, and triethylamine hydrochloride was precipitated. After 3 hr., the hydrochloride was filtered off and the filtrate was washed with dilute hydrochloric acid, twice with N-sodium hydroxide, and finally with water, filtered, and evaporated *in vacuo*. The residue (1·12 g.), recrystallised twice from ether–ethyl acetate with light petroleum (b. p. 40—60°), gave plates, m. p. 84—85° (Found, in material dried *in vacuo* at 50°: C, 71·7; H, 5·1; P, 5·7%).

Quinol Dibenzyl (and Benzyl Ethyl) Phosphate.—By the method described for the preparation of 2-methyl-1,4-naphthaquinol 1-(dibenzyl phosphate) a number of analogous compounds were prepared (see Table 1).

TABLE 1. *Quinol phosphates.*

Compound	Reaction in	Recryst. from [d]	M. p.	Yield (%)	Found (%) C	H	P	Formula	Required (%) C	H	P
2,3-Dimethyl-1,4-naphthaquinol 1-(dibenzyl phosphate)	MeCN	EtOAc–Pet	111—112·5°	82	70·0	5·6	7·0	$C_{26}H_{25}O_5P$	69·6	5·6	6·9
,, ,, 1-(benzyl ethyl phosphate)	MeCN	CCl_4	111—112	49	65·2	5·9	8·2	$C_{21}H_{23}O_5P$	65·5	6·0	8·0
Quinol 1-(dibenzyl phosphate)	C_6H_6	EtOAc–Pet	84—86	51	64·9	5·0	8·4	$C_{20}H_{19}O_5P$	64·9	5·2	8·4
,, ,, 1-(benzyl ethyl phosphate)	MeCN		46—51	92	58·8	5·4	9·6	$C_{15}H_{17}O_5P$	58·4	5·6	10·1
Trimethylquinol 1-(dibenzyl phosphate)	MeCN	EtOAc–Pet	100—101	52·9 [b]	67·0	5·7	7·7	$C_{22}H_{23}O_5P$	67·0	6·1	7·5
Duroquinol 1-(dibenzyl phosphate)	MeCN	,,	112—113	81·5	67·6	6·2	7·2	$C_{24}H_{27}O_5P$	67·7	6·4	7·3
Tetrachloroquinol 1-(dibenzyl phosphate)	C_6H_6	,,	143—145	33	47·6	2·6	—	$C_{20}H_{15}Cl_4O_5P$	47·5	3·0	—
,, ,, 1-(benzyl ethyl phosphate)	PhMe	,,	137—139	22	40·3	3·1	7·0	$C_{15}H_{13}Cl_4O_5P$	40·4	2·9	7·0

[a] Purified by extraction of an ethereal solution with N-potassium hydroxide followed by acidification of the alkaline extracts and extraction of the product with chloroform. [b] Total yield of a colourless crystalline mixture of 1- and 4-phosphates (m. p. 75—83°). Fractional crystallisation gave a single pure phosphate, m. p. 100—101°. [c] Under reflux for 3 hr. [d] Pet = light petroleum (b. p. 40—60°).

2,3-Dimethyl-1,4-naphthaquinol 4-Acetate 1-(Dibenzyl Phosphate).—To 2,3-dimethyl-1,4-naphthaquinol 1-(dibenzyl phosphate) in acetic anhydride, a catalytic amount of sulphuric acid (yield

[15] Lindlar, U.S.P. 2,839,570.

86%) or triethylamine (yield 91%) was added. The *product* formed needles, m. p. 105—106° (Found, in material dried *in vacuo* at 60°: C, 68·8; H, 5·1; P, 6·7. $C_{28}H_{27}O_6P$ requires C, 68·7; H, 5·6; P, 6·3%).

The *4-toluene-p-sulphonate*, prepared in 2,6-lutidine, had m. p. 88—89·5° (Found, in material dried *in vacuo* at 40°: C, 61·9; H, 4·7; P, 5·7; S, 6·2. $C_{27}H_{25}O_7PS$ requires C, 61·8; H, 4·8; P, 5·9; S, 6·1%), and had no infrared hydroxyl and carbonyl band.

Quinol Mono(dihydrogen Phosphates) and Mono(ethyl Hydrogen Phosphates).—The quinol dibenzyl phosphates and benzyl ethyl phosphates, described above, were hydrogenolysed in ethanol with 10% palladium–charcoal. The theoretical or nearly theoretical volume of hydrogen was absorbed and after removal of the catalyst the residual acid ester was recrystallised. The yields were virtually theoretical and depended upon the efficiency of the crystallisation. Salts were prepared by the addition of base to the acid in alcohol. Data for the *compounds* prepared are given in Tables 2 and 3.

2-Methyl-3-phytyl-1,4-naphthaquinol 1-(Dibenzyl Phosphate) [*Dihydrovitamin K_1 1-(Dibenzyl Phosphate)*].—To a solution of vitamin K_1 (4·5 g.) in benzene, stirred under nitrogen, was added dibenzyl phosphite (3·0 g., 1·15 mole) in benzene (2 ml.) followed by 1·1N-potassium t-butoxide in t-butyl alcohol (1 ml.) containing 10% of benzene. The mixture became warm and was cooled for a few minutes, then stirred at room temperature for 2 hr., diluted with light petroleum (b. p. 40—60°), filtered, and washed with water, dilute hydrochloric acid, water, and finally

TABLE 2. *Dihydrogen phosphates and their monoethyl esters.*

			Found (%)				Required (%)			Mol. wt.[f]	
No.	Quinol	M. p.	C	H	P	Formula	C	H	P	Found	Req.
1	2,3-Dimethyl-1,4-naphthaquinol	128—129°[a]	53·8	5·35	11·7	$C_{13}H_{13}O_5P$	53·6	4·9	11·6	272	268
2	,, ,, 4-acetate	185—188°[b]	54·5	4·5	9·6	$C_{14}H_{15}O_6P$	54·2	4·9	10·0	314	310
3	,, ,, Et ester	165—166[c]	56·9	5·7	10·6	$C_{14}H_{17}O_5P$	57·0	5·8	10·2	296	296
4	2-Methyl-1,4-naphthaquinol (1-phosphate)	194—195°[b]	51·4	4·9	11·9	$C_{11}H_{11}O_5P$, $0·25H_2O$	51·1	4·5	12·0	262	259
5	,, (4-phosphate)[5]	150°[d]	—	—	11·7	$C_{11}H_{11}O_5P$	—	—	12·2	255	254
6	Quinol	167—168·5[b]	38·4	3·9	16·2	$C_6H_7O_5P$	37·9	3·7	16·3	197	190
7	,, Et ester	Oil	43·7	5·4	14·5	$C_8H_{11}O_5P$	44·0	5·1	14·2		
8	Trimethylquinol	211—212[e]	47·0	5·3	13·3	$C_9H_{13}O_5P$	46·5	5·6	13·3		
9	Duroquinol	237°[e]	48·4	5·8	12·2	$C_{10}H_{15}O_5P$	48·8	6·1	12·6	252	246
10	Tetrachloroquinol	204—206°	21·8	1·35	9·1	$C_6H_2Cl_4O_5P$, $0·5H_2O$	21·4	1·2	9·2		
11	,, Et ester	224—225°[e]	27·9	2·3	8·3	$C_8H_7Cl_4O_5P$	27·0	2·0	8·7		

° With decomp. [a] From EtOAc–cyclohexane. [b] From EtOAc–Pet (Pet = light petroleum of b. p. 40—60°). [c] As *b* but with 5% of MeOH. [d] From Et_2O–Pet. [e] From cyclohexane. [f] By titration.

TABLE 3. *Salts of phosphates.*

Ref. from Table 2	Salt	Recryst. from	M. p.	Found (%) C	H	P	Formula	Required (%) C	H	P
No. 1	Cyclohexylammonium	MeOH–Et_2O	200—203°	60·3	8·1	7·0	$C_{12}H_{13}O_5P$, $1·5C_6H_{12}N$	60·5	7·9	7·4
4-Ac deriv. of No. 4	Anilinium	EtOH–Et_2O	190—191	58·9	5·2	7·8	$C_{19}H_{20}NO_6P$	58·6	5·2	8·0
,,	Triethylammonium	EtOAc–Pet	211—212	57·8	7·4	8·4	$C_{19}H_{28}NO_6P$	57·4	7·2	8·7
1-Ac deriv. of No. 5	Anilinium	EtOH	180—182	57·4	5·1	8·3	$C_{19}H_{20}NO_6P$, $0·5H_2O$	57·3	5·3	7·8
No. 6	Anilinium	EtOH	176—177	51·0	5·0	10·5	$C_{12}H_{14}NO_5P$	50·9	5·0	10·9
No. 7	Cyclohexylammonium	MeOH–Et_2O	175—178	52·6	7·8	9·6	$C_{14}H_{24}NO_5P$	53·0	7·6	9·8
No. 9	Cyclohexylammonium	MeOH–Et_2O–Pet	214—218	55·7	7·9	9·3	$C_{14}H_{28}NO_5P$	55·7	8·2	9·0

twice with 90% methanol (to remove any unreacted dibenzyl phosphite). The petroleum layer was dried (Na_2SO_4) and evaporated *in vacuo*, leaving the *ester* as a pale yellow oil (6·86 g., 97%) (Found: C, 75·6; H, 8·8; P, 5·0. $C_{45}H_{61}O_5P$ requires C, 75·8; H, 8·6; P, 4·4%).

This phosphate (3·55 g.) with benzoyl chloride–pyridine at room temperature (2 hr.) gave

an oil (3·76 g.) which was chromatographed on alumina pretreated with methyl formate, elution being with light petroleum (b. p. 80—100°), 1 : 1 light petroleum–benzene, and finally benzene. The petroleum–benzene eluate, on evaporation *in vacuo*, gave *2-methyl-3-phytyl-1,4-naphthaquinol 4-benzoate 1-(dibenzyl phosphate)* as a colourless oil (2·3 g.) (Found: C, 76·2; H, 7·7; P, 4·1. $C_{52}H_{65}O_6P$ requires C, 76·4; H, 8·0; P, 3·8%).

The *propionate* was prepared in pyridine and similarly chromatographed, forming a practically colourless oil (76% yield) (Found: C, 74·3; H, 8·4; P, 4·4. $C_{48}H_{65}O_6P$ requires C, 75·0; H, 8·3; P, 4·0%).

2-Methyl-3-phytyl-1,4-naphthaquinol 1-Benzoate 4-(Dibenzyl Phosphate).—Dihydrovitamin K_1 1-benzoate [15] (10·0 g.) was dissolved in dry carbon tetrachloride (15 ml.) and dibenzyl phosphite (5·0 g.) was added. The solution was cooled in ice-water and dry triethylamine (2·55 ml.) was added slowly with shaking. The base hydrochloride separated and after ½ hr. the mixture was set aside at room temperature overnight. The hydrochloride was filtered off and the filtrate was evaporated to an oil which was washed in ether with N-sodium hydroxide and then twice with water (sodium sulphate added to break emulsions), dried (Na_2SO_4) and recovered. A 68% yield of the crude *4-(dibenzyl phosphate)* was obtained which was purified by chromatography on neutral alumina as described for the 1-(dibenzyl phosphate) (Found: C, 77·2; H, 8·1; P, 4·1%).

2-Methyl-3-phytyl-1,4-naphthaquinol 1-(Dihydrogen Phosphate).—Dihydrovitamin K_1 1-(dibenzyl phosphate) (2 g.) was hydrogenolysed in absolute ethanol (20 ml.) with 10% palladium–charcoal (200 mg.) (which did not hydrogenate dihydrovitamin K_1 or its 1-benzoate). Uptake (theor.) ceased in 50 min. After removal of the catalyst the alcohol was evaporated off *in vacuo*, to give a hygroscopic oily *acid* which became reddish-brown (Found: C, 69·9; H, 9·8; P, 5·4. $C_{31}H_{49}O_5P$ requires C, 70·0; H, 9·3; P, 5·8%). A paper chromatogram of this product on Whatman no. 1 paper impregnated with silicone fluid (dipped in a 10% solution of silicone fluid in light petroleum and dried) with ethanol–water–acetic acid (2 : 1 : 1) (ascending, 17 hr. at room temperature) showed one major spot (R_F 0·88, visible under ultraviolet light and phosphate-containing), a faint trail (R_F 0—0·1, visible under ultraviolet light, corresponding to vitamin K_1), and a small faint spot (R_F 0·62, inorganic phosphate). The product, in water, had $\lambda_{max.}$ 242, 272, $\lambda_{min.}$ 230, 257 mμ (ε 40,000, 5750 27,750, and 4750, respectively). The infrared spectrum confirmed the presence of hydroxyl and phosphate groups. This acid formed a solid *anilinium salt* of indefinite m. p. (Found, in material dried *in vacuo*: C, 71·4; H, 8·9; N, 2·5; P, 5·2. $C_{37}H_{56}NO_5P$ requires C, 71·0; H, 9·0; N, 2·2; P, 5·0%), $\lambda_{max.}$ 240 mμ (ε 63700) in H_2O.

Dihydrovitamin K_1 4-Acetate 1-(Dihydrogen Phosphate).—Dihydrovitamin K_1 1-(dibenzyl phosphate) (1·5 g.) was kept for 2 hr. in acetic anhydride (6 ml.) containing a trace of concentrated sulphuric acid. The product, worked up as usual and hydrogenolysed as above, gave the *4-acetate 1-(dihydrogen phosphate)* (86%) as a faintly orange oil (Found, in material dried *in vacuo*: C, 66·7; H, 9·0; P, 4·5. $C_{33}H_{51}O_6P,H_2O$ requires C, 66·9; H, 9·0; P, 5·2%), $\lambda_{max.}$ 232 mμ (ε 52,600) in H_2O. The infrared spectrum confirmed the acetate grouping.

Dihydrovitamin K_1 1-(dihydrogen phosphate) 4-propionate, prepared by hydrogenolysis of its dibenzyl ester, was an amber-coloured oil (99% yield) (Found, in material dried *in vacuo*: C, 68·2; H, 9·4; P, 6·0. $C_{34}H_{53}O_6P,0{\cdot}5H_2O$ requires C, 68·3; H, 9·1; P, 5·2%). Adding methanolic ammonia to its solution in ethanol caused precipitation of the *diammonium salt* which was completed by adding acetonitrile. This had m. p. 160° after softening at 152° (Found, in material dried *in vacuo*: C, 65·4; H, 9·5; N, 4·4; P, 5·0. $C_{34}H_{59}N_2O_6P$ requires C, 65·6; H, 9·6; N, 4·5; P, 4·9%), $\lambda_{max.}$ 237 mμ (ε 62,280) in water.

Dihydrovitamin K_1 4-Benzoate 1-(Anilinium Hydrogen Phosphate).—Dihydrovitamin K_1 4-benzoate 1-(dibenzyl phosphate) (0·5 g.) was hydrogenolysed in absolute ethanol (5 ml.) with 10% palladium–charcoal catalyst (50 mg.) (theoretical uptake in 20 min.). After removal of the catalyst, aniline (0·3 ml.) in a little ethanol was added, followed by acetonitrile to turbidity. The precipitated *aniline salt* (200 mg.) had m. p. 146—147° (from ethanol–acetonitrile) (Found, in material dried *in vacuo* at 80°: C, 72·6; H, 8·1; N, 1·8; P, 4·2. $C_{44}H_{60}NO_6P$ requires C, 72·4; H, 8·3; N, 1·9; P, 4·2%). A paper chromatogram (system A; descending, 17 hr.) gave a single spot R_F 0·89, absorbing ultraviolet light and containing phosphate. The mixed m. p. with the isomer prepared as below was 135—149°; the infrared spectra were practically identical, except in the phosphate band region.

Dihydrovitamin K_1 1-benzoate 4-(anilinium hydrogen phosphate), prepared similarly, had

m. p. 160—161° (from ethanol–acetonitrile) (Found, in material dried *in vacuo* at 80°: C, 72·7; H, 8·2; N, 1·9; P, 4·2%). On paper chromatography it behaved as its isomer but had R_P 0·9.

Dihydrovitamin K_1 1-(*Ethyl Hydrogen Phosphate*).—Vitamin K_1 (2·5 g.) and benzyl ethyl phosphite (1·2 g.) were treated in benzene (25 ml.) with 0·4N-potassium t-butoxide (1 ml.) in 9 : 1 t-butyl alcohol–benzene. After 2 hr. at room temperature the mixture was washed with sodium sulphate solution, filtered, and dried (Na_2SO_4). Evaporation, finally at 40°/0·1 mm., gave dihydrovitamin K_1 1-(benzyl ethyl phosphate) as a pale yellow oil (3·14 g., 87%). This was hydrogenolysed, as above, to a light brown oil (2·54 g.) which a paper chromatogram indicated as being mainly the required *product* but containing a little vitamin K_1 and another organic phosphate. It was dissolved in ether (30 ml.) and extracted with dilute potassium hydroxide solution (2 × 30 ml.). The alkaline layers were washed with ether, then acidified with dilute hydrochloric acid and extracted with ether. The ether layer was washed with water, dried (Na_2SO_4), and evaporated, finally at 60°/0·1 mm. A light brown oil (1·04 g.) remained (Found: C, 71·4; H, 9·6; P, 5·6. $C_{33}H_{53}O_5P$ requires C, 70·7; H, 9·5; P, 5·5%). A paper chromatogram (system A; ascending, 17 hr.) showed a single spot (R_P 0·92) which absorbed ultraviolet light and contained phosphate.

Dihydrovitamin K_1 1-(*Ethyl Hydrogen Phosphate*) 4-(*Dihydrogen Phosphate*).—N-Potassium t-butoxide (*ca.* 0·3 ml.) was added dropwise to a solution of vitamin K_1 (1·0 g.) and benzyl ethyl phosphite (0·5 g.) in dry benzene (2·5 ml.) until no further reaction occurred. After the mixture had been set aside for 1 hr., dry pyridine (10 ml.) was added and the solution was cooled in ice-water. Next was added a cold solution of phosphorus oxychloride (2·2 ml.) in dry pyridine (10 ml.) and the whole was left for ½ hr. at room temperature. The solvent and excess of oxychloride were removed *in vacuo*, dry toluene was added, and the solution was again evaporated *in vacuo*. The residue was partitioned between ether (40 ml.) and water (40 ml.), and the ether layer was washed successively with water (40 ml.), N-potassium hydroxide (2 × 40 ml.), N-hydrochloric acid (40 ml.), and dilute sodium sulphate solution, filtered, dried (Na_2SO_4), and evaporated, finally at 60°/0·1 mm. for 1 hr. Dihydrovitamin K_1 1-(benzyl ethyl phosphate) 4-(dihydrogen phosphate) remained as a pale yellow oil (1·42 g., 88%). This was hydrogenolysed in ethanol (30 ml.) with palladium–charcoal (0·2 g.) for 1 hr. (uptake, 46·7 ml.). After removal of the catalyst evaporation (finally at 60°/0·1 mm. for 2 hr.) gave the *di*(*phosphate*) as a pale yellow oil (1·04 g.) (Found: C, 62·5; H, 8·4; P, 9·8. $C_{33}H_{54}O_8P_2$ requires C, 61·9; H, 8·5; P, 9·7%). A paper chromatogram (system A; ascending, 17 hr.) showed a single spot, R_P 0·73—0·97, absorbing ultraviolet light and containing phosphorus, that had $\lambda_{max.}$ 234 and 290 (ε 63,000 and 4950), $\lambda_{min.}$ 254 mμ (ε 1250), in EtOH.

In another experiment, with 10 g. of vitamin K_1, methanolic ammonia was added to the final solution, after hydrogenolysis, and the amorphous *diammonium salt* of dihydrovitamin K_1 1-(ethyl hydrogen phosphate) 4-(dihydrogen phosphate) (11·4 g.; 74%) was precipitated with acetonitrile (Found, in material dried *in vacuo*: C, 59·1; H, 8·9; N, 3·8; P, 9·5. $C_{33}H_{60}N_2O_8P_2$ requires C, 58·7; H, 9·0; N, 4·2; P, 9·2%).

2-Geranyl-3-methyl-1,4-naphthaquinol (*Ammonium Hydrogen Phosphate*) (*Dihydrovitamin* $K_{2(10)}$ *Ammonium Hydrogen Phosphate*).—Dihydrovitamin $K_{2(10)}$ dibenzyl phosphate, prepared by the method given for dihydrovitamin K_1 1-(dibenzyl phosphate) was hydrogenolysed in ethanol with Lindlar's palladium–barium sulphate catalyst. Absorption was slow and ceased with 82% of the theoretical value. The acid ester obtained was impure but an *ammonium salt* was prepared which on a paper chromatogram (system A; ascending, 17 hr.) had R_P 0·88 and showed only two faint spots for impurity (Found, in material dried *in vacuo*: N, 3·5; P, 7·5. $C_{21}H_{30}NO_5P$ requires N, 3·4; P, 7·6%).

α-*Tocopherylquinol Mono*(*dihydrogen Phosphate*).—α-Tocopheryl quinone was converted into the *mono*(*dibenzyl phosphate*) (2·24 g.) by the method given for dihydrovitamin K_1 (Found: C, 73·3; H, 8·8. $C_{43}H_{65}O_6P$ requires C, 72·9; H, 9·2%). The pale oil (1·88 g.) was hydrogenolysed in the usual way (uptake 127 ml. in 1 hr.). An ethereal solution of the impure acid ester obtained was extracted with dilute potassium hydroxide solution; acidification of the alkaline solution and extraction of the *acid ester* with ether gave a faintly orange-coloured oil (60·5%) (Found, in material dried *in vacuo*: C, 66·2; H, 10·3; P, 5·4. $C_{29}H_{53}O_6P$ requires C, 65·9; H, 10·1; P, 5·9%). A paper chromatogram (system A; ascending, 17 hr.) showed a single absorbent spot under ultraviolet light (R_F 0·93) but there was a trace of phosphate impurity (R_F 0·56). Ultraviolet light absorption in ethanol was min. at 254 mμ (ε 660) and max. at 282 mμ (ε 1760).

Vol. 1961, page 1815, line 1. Replace paragraph beginning *Ubiquinol*$_{(50)}$ *Mono(dibenzyl phosphate)* by these two paragraphs:

Ubiquinol$_{(50)}$ *Mono(dibenzyl Phosphate)*.—Ubiquinone$_{(50)}$ (0·65 g.) was dissolved in benzene (1 ml.) under nitrogen while dibenzyl phosphite (0·24 g., 1·2 equiv.) in benzene (0·5 ml.) was added, followed by N-potassium t-butoxide in t-butyl alcohol–10% benzene (0·1 ml.). The dark solution became warm and practically decolorised. After being stirred for 1 hr. at room temperature, the mixture was diluted with ether and washed with water ($MgSO_4$ added to break the emulsion), 0·2N-hydrochloric acid, and water. After filtration, the ethereal solution

was dried ($MgSO_4$) and evaporated, finally *in vacuo*. The residual colourless, oily ubiquinol mono(dibenzyl phosphate) (0·83 g.) crystallised on prolonged keeping, then having m. p. 37—45° (Found, in material dried *in vacuo:* C, 76·9; H, 9·5; P, 2·4. $C_{73}H_{105}O_7P$ requires C, 77·9; H, 9·4; P, 2·5%).

Ubiquinol$_{(50)}$ *Mono(dihydrogen Phosphate)*.—Ubiquinol dibenzyl phosphate (2·38 g.) in ethanol (30 ml.) was left at room temperature over charcoal (100 mg.)–Lindlar catalyst (100 mg.) for 1 hr. The solution was filtered and hydrogenolysed in presence of Lindlar catalyst (200 mg.). The theoretical volume of hydrogen (102 ml.) was absorbed in 19 hr., two further additions of catalyst being necessary (in another experiment hydrogenolysis was complete in 5 hr.). After removal of the catalyst, by filtration, the solution was evaporated *in vacuo*, and then at 40°/0·1 mm for 3 hr. The residue (1·75 g.) eventually formed waxy crystals, m. p. *ca.* 40° (Found, C, 74·5; H, 9·8; P, 3·0. $C_{59}H_{93}O_7P$ requires C, 74·9; H, 9·9; P, 3·3%), $\lambda_{min.}$ (in EtOH) 250 mμ (ε 370), $\lambda_{max.}$ 282 mμ (ε 2,280). The compound was soluble in most common solvents and in dilute alkali. Paper chromatography on Whatman no. 1 paper previously treated with a 10% Silicone fluid in light petroleum, with ethanol–water–acetic acid (2:1:1) as solvent (ascending; 16 hr.; room temperature) gave a single ultraviolet-light-absorbent and phosphate spot of R_P 0·86. Use of Whatman 3 MM paper [treated with a 5% silicone fluid solution; propan-1-ol–water (4:1); ascending, 15 hr.; room temperature [1]] gave a single ultraviolet light absorbent and phosphate spot of R_P 0·87 (ubiquinone$_{(50)}$ has R_P 0·3).

Ref.: [1] Lester and Ramasarma, *J. Biol. Chem.*, 1959, 234, 672.

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Ubiquinol$_{(50)}$ Mono(dibenzyl Phosphate).—Ubiquinone$_{(50)}$ (0·65 g.) was stirred in benzene (1 ml.) under nitrogen while dibenzyl phosphite (0·24 g., 1·2 equivalents) in benzene (0·5 ml.) was added, followed by dilute alkali (a gel formed first). Paper chromatography on Whatman no. 1 paper [treated with a 10% silicone fluid solution in light petroleum; ethanol–water–acetic acid (2 : 1 : 1); ascending, 16 hr.; room temperature] gave a single spot (R_F 0·86) absorbing ultraviolet light and containing phosphate. System A (except that 4 : 1 propan-1-ol–water was used; ascending, for 15 hr.) [16] gave a single, similar spot of R_F 0·87 (ubiquinone$_{(50)}$ has R_F 0·3).

Benzyl Ethyl Phosphite.—A solution of benzyl alcohol (84 ml., 88·3 g.) and diethylaniline (65 ml., 60·8 g.) was added dropwise, during 30 min., to a stirred solution of ethyl phosphorodichloridite (60 g.) in dry benzene (350 ml.) at 5—10° (freezing mixture). The mixture was then stirred for 2 hr. at 0°, water (140 ml.) was added, and the mixture stirred for a further hour. The benzene solution was washed with water (3 × 140 ml.), 3N-ammonia (3 × 250 ml.), and water (3 × 140 ml.), filtered, dried ($MgSO_4$), and evaporated, finally at 100°/0·35 mm. The residue was distilled and the fraction of b. p. 94—107°/0·35 mm. was collected. This *ester*, redistilled through a short column, had b. p. 108—110°/0·35 mm., n_D^{20} 1·5024 (27·3 g., 35%) (Found: C, 53·9; H, 6·9; P, 16·1. $C_9H_{13}O_3P$ requires C, 54·0; H, 6·6; P, 15·5%).

Adenosine 5′-Phosphate.—Crude 2′,3′-isopropylideneadenosine benzyl phosphite [13] (12·3 g.) was treated in dry benzene (40 ml.) with 2,3-dimethyl-1,4-naphthaquinone (4·95 g.) followed by N-potassium t-butoxide in 9 : 1 t-butyl alcohol–benzene (2 ml.) in small portions. After the mixture had been stirred for 1½ hr. it was set aside overnight. Most of the benzene was evaporated off and chloroform was added to the residue. The chloroform solution was washed with water, 0·01N-hydrochloric acid, and water, filtered, evaporated to small bulk, and poured into ether. Crude 2′,3′-*O*-isopropylideneadenosine 5′-(benzyl-4-hydroxy-2,3-dimethylnaphthyl phosphate) (11·0 g.) separated as an oil which solidified on trituration with ether. Part of the material (3·24 g.) was refluxed in dry ethyl methyl ketone (16 ml.) with sodium thiocyanate (0·44 g.) for 2 hr. An oil (1·78 g.) (A) separated which solidified and was collected, washed with acetone, and dried. A second crop (0·88 g.) was obtained from the ethyl methyl ketone mother-liquors. The first crop was dissolved in water and acidified, giving an amorphous precipitate (1·15 g.). Attempted recrystallisation of this precipitate from acetic acid gave an apparently amorphous *substance* (B) of indefinite m. p. (cleared at 160—165°) (Found, in material dried *in vacuo*: C, 50·6; H, 5·1; N, 11·3; P, 4·8. $C_{25}H_{28}N_5O_8P,2H_2O$ requires C, 50·6; H, 5·4; N, 11·8; P, 5·2%). A paper chromatogram (system B) gave a single fluorescent spot (ultraviolet light) (R_F 0·77). Addition of bromine water to a solution of the sodium salt (A) gave an immediate precipitate of 2,3-dimethylnaphthaquinone, m. p. and mixed m. p. 122—123°. The acid (B) (237 mg.) was suspended in water, and 0·098N-sodium hydroxide was added to give a solution of pH 8·4. Oxygen was bubbled through this and the pH was maintained at 8·4—9·6 by further additions. During *ca.* 10 hr. 3·8 ml. of the alkali were required (theor. 4·3 ml.). A paper chromatogram indicated that 2′,3′-isopropylideneadenylic acid was the main product. 0·1N-Hydrochloric acid (9 ml.) was added and the solution was heated on a boiling-water bath for 20 min. A paper chromatogram (Whatman no. 4 paper; 6 : 3 : 1 propan-1-ol–ammonia–water; ascending, 2 hr. at room temperature) showed a trace of isopropylideneadenylic acid, R_F 0·52, adenylic acid, R_F 0·27 (authentic, R_F 0·25), a trace of inorganic phosphate, R_F 0·16, and two small spots (fluorescent in ultraviolet light but not containing phosphate), R_F 0·8 and 0·97 (probably 2,3-dimethylnaphthaquinone and a related substance). The solution was evaporated to small bulk and a little acetone added. A small amount of precipitated brown oil solidified later. Further addition of acetone gave colourless crystals (18·5 mg.), m. p. 169—171° (decomp.). Recrystallisation from water, with the addition of a little acetone, raised the m. p. to 186—188° (decomp.) undepressed on admixture with muscle adenylic acid of m. p. 192° (decomp.).

Phosphorylation of Ethanol.—(*a*) 2,3-Dimethyl-1,4-naphthaquinol 1-(dihydrogen phosphate) (0·4 g.), palladium–charcoal (0·1 g.), anhydrous calcium sulphate (0·2 g.), and triethylamine (0·5 ml.) in dry ethanol (20 ml.) were shaken in oxygen. After the theoretical uptake (18 ml.) the catalyst was filtered off and a drop of the filtrate (now bright yellow owing to 2,3-dimethylnaphthaquinone) was paper chromatographed (system B). Spots of authentic material showed the presence of 2,3-dimethylnaphthaquinone (R_F 0·93), ethyl phosphate (R_F 0·48), and traces of 2,3-dimethylnaphthaquinol monophosphate (R_F 0·69) and inorganic phosphate (R_F 0·36).

[16] Lester and Ramasarma, *J. Biol. Chem.*, 1959, **234**, 672.

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The ethyl phosphate was isolated as the monoanilinium salt, m. p. and mixed m. p. 166—168°.

(*b*) Dihydrovitamin K_1 1-phosphate (0·5 g.), palladium–charcoal (0·1 g.), anhydrous copper sulphate (0·2 g.), and dry triethylamine (0·5 ml.) in dry ethanol (20 ml.) were shaken under oxygen at room temperature for 1½ hr. during which time only 5 ml. of oxygen were absorbed.

TABLE 4. *Stability data for 0·2% solutions in aqueous buffer.*

Compound	pH	Temp.	Time (hr.)	Release (%) of phosphate in N_2	Release (%) of phosphate in O_2
2-Methyl-1,4-naphthaquinol 1-phosphate	8·4	37°	2	—	8·2
	8·4	37	4	—	20·6
2-Methyl-1,4-naphthaquinol 4-phosphate	8·4	37	10	—	61·4
	8·4	37	30	4·1	100·5
2-Methyl-1,4-naphthaquinol 4-acetate 1-phosphate	8·4	37	4	<1	<1
2-Methyl-1,4-naphthaquinol 1-acetate 4-phosphate	8·4	37	4	3·7	8·9
2,3-Dimethyl-1,4-naphthaquinol 1-phosphate	3·5	38	4	12·0	21·3
	6·4	38	4	8·3	44·0
	7·5	38	4	9·0	70·0
	9·9	38	4	39·0	94·5
Dihydrovitamin K_1 1-phosphate	7·7	38	4	11·4	45·2
Dihydrovitamin K_1 4-acetate 1-phosphate	7·7	38	4	3·2	5·1
	8·3	38	4	3·5	6·0
Duroquinol 1-phosphate	8·3	37	4	—	2·5
Ubiquinol$_{(50)}$ monophosphate	8·4	37	4	2·2	4·1

The temperature was raised to 60° and in a further 1½ hr. 13 ml. of oxygen were absorbed and then the absorption practically ceased (theor., 21 ml.). The solution was filtered and part of it was partially evaporated and chromatographed (system A; ascending, 17 hr.). The following spots were observed; R_F 0·21, absorbent in ultraviolet light (R_F of vitamin K_1); R_F 0·42, phosphate-containing; R_F 0·66, phosphate-containing (R_F of triethylammonium ethyl phosphate); R_F 0·69, absorbent in ultraviolet light; R_F 0·73—0·94, absorbent in ultraviolet light and phosphate-containing (R_F of dihydrovitamin K_1 monophosphate). A little of the solution was acidified with dilute hydrochloric acid and heated at 100° for 10 min. to decompose any pyrophosphates present. A paper chromatogram, obtained as previously, only then showed 3 spots: R_F 0·14, absorbent in ultraviolet light (R_F of vitamin K_1); R_F 0·78, a phosphate (R_F of ethyl dihydrogen phosphate); and R_F 0·93, ultraviolet light-absorbent and phosphate-containing (R_F of dihydrovitamin K_1 monophosphate). It was concluded that ethyl phosphate had been formed together with at least one and possibly two pyrophosphates.

Stability Data.—The results in Table 4 are self-explanatory.

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351. *The Dissociation Constants of Some Chlorides and Perchlorates in Aqueous Acetone from Conductance Measurements.*

By V. M. Atkins and C. B. Monk.

The dissociation constants of HCl, LiCl, NaCl, $HClO_4$, and $NaClO_4$ in 80% and 90% aqueous acetone (by vol.) at 25° have been estimated from their conductances by various treatments. According to these, perchloric acid and sodium perchlorate are completely dissociated. Some spectrophotometric measurements support this view concerning perchloric acid in 80% acetone but not for the 90% solvent.

In a recent report [1] on some conductances in aqueous dioxan, it was concluded that hydrogen, sodium, and potassium chlorides are weak electrolytes when the dioxan content exceeds about 60%. The values of the derived dissociation constants were shown to be slightly dependent upon the treatments used to analyse the data and this is further illustrated by the results reported here where the solvent is aqueous acetone. The methods of (*a*) Davies,[2] (*b*) Fuoss and Kraus (1933),[3] (*c*) Robinson and Stokes,[4] and (*d*) Fuoss (1959)[5] have been used; the first two of these treat ions as point charges and the second two incorporate an ion-size parameter. To be consistent, the limiting and the extended form of the Debye–Hückel activity coefficient expression were taken for (*a*,*b*) and (*c*,*d*) respectively, while the Λ_0 values were selected on the basis that the dissociation constants K should be sensibly constant over the concentration ranges investigated. For these reasons individual values of $K(b)$ and $K(d)$ were calculated for each concentration in preference to the usual plotting procedures.

The conductances of both sodium perchlorate and perchloric acid in 80% and 90% acetone proved to be markedly higher than those calculated by the limiting Onsager equation if dissociation is complete, but by choosing appropriate values of Λ_0 and the ion-size parameter *a*, both Robinson and Stokes's equation [4] and Fuoss's *J* equation [5] can reproduce the experimental values within close limits. On the other hand, while there is evidence [6] that perchlorates are stronger electrolytes than the corresponding chlorides, it is doubtful if perchloric acid and sodium perchlorate ionise completely in 90% acetone. To obtain some independent information, solutions of hydrochloric and of perchloric acid were matched spectrophotometrically by means of *m*-Cresol Purple. These measurements confirmed that perchloric acid is very strongly dissociated in 80% acetone but if the value of K_{HCl} from Table 1 is accepted, then perchloric acid does associate in the 90% solvent. Some figures for K_{HClO_4} are given in Table 2; the value of $[H^+]$ in each HCl solution was obtained by approximations, being taken as 4·0 Å when calculating activity coefficients.

The main conclusions which can be drawn from these comparative sets of calculations are that there are only minor differences between the derived dissociation constants by the different treatments, and that the interpretation of the conductances of perchloric acid and sodium perchlorate in the selected solvents is not completely acceptable. The dissociation constants of the chlorides as obtained by the method of Robinson and Stokes,[4] *i.e.*, $K(c)$, are slightly lower than the other sets of figures in Table 1, and this agrees with what was found when the solvent is aqueous dioxan.[1] It is noteworthy that the limiting conductance equation seems to function for the chlorides but not for the perchlorates unless the ion-size parameter is introduced, but a very large value of this would be needed to obtain a value for K_{HClO_4} from the conductances in 90% acetone to match that shown by Table 2. On the other hand, since $\Lambda_0(HClO_4) > \Lambda_0(HCl)$ in the present solvents and

[1] Nash and Monk, *Trans. Faraday Soc.*, 1958, **54**, 1650.
[2] Davies, *Trans. Faraday Soc.*, 1927, **23**, 351.
[3] Fuoss and Kraus, *J. Amer. Chem. Soc.*, 1933, **55**, 476; Fuoss, *ibid.*, 1935, **57**, 488.
[4] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 2nd edn., 1959.
[5] Fuoss, *J. Amer. Chem. Soc.*, 1959, **81**, 2659.
[6] "Stability Constants," Part II, *Chem. Soc. Special Publn.* No. 7, 1957.

XUM

$\Lambda_0(NaClO_4) > \Lambda_0(NaCl)$ in 80% acetone, these suggest that the radius of the Cl^- ion is greater than that of ClO_4^-. This is contradicted, not only by crystallographic data, but also by a comparison of the conductances of these two anions in water.[4] The answers to these puzzles may emerge from further similar studies and analyses.

TABLE 1. *Conductances and dissociation constants of* HCl, LiCl, NaCl, $HClO_4$, *and* $NaClO_4$ *in aqueous acetone at* 25°.

(Methods *a*, *b*, *c*, and *d* are as noted on p. 1817, the last using the extended Fuoss–Onsager conductance theory.)

HCl; aq. acetone, 90% by vol. = 87·6% by wt.; $\varepsilon = 25{\cdot}3$; $\eta = 0{\cdot}00457$.

		$10^4c =$	2·016	2·467	4·446	5·408	6·324	7·172	8·874	11·779	
a (Å)	Λ_0	$\Lambda =$	97·52	96·26	91·31	89·13	87·48	85·88	83·19	79·33	
0	107·60	$10^3K(a) =$	2·94	2·99	3·04	2·96	2·98	2·96	2·93	2·92	Av. = 2·97 ± 0·05
0	107·60	$10^3K(b) =$	2·91	2·99	3·02	2·95	2·98	2·93	2·92	2·92	Av. = 2·95 ± 0·05
4·0	107·60	$10^3K(c) =$	2·88	2·94	2·96	2·89	2·89	2·88	2·89	2·86	Av. = 2·90 ± 0·03
4·0	107·70	$10^3K(d) =$	3·02	3·10	3·11	3·04	3·08	3·03	3·01	3·00	Av. = 3·05 ± 0·03

LiCl (90%).

		$10^4c =$	2·631	3·784	5·764	8·503	12·067	17·178	18·778	21·532	
a (Å)	Λ_0	$\Lambda =$	87·52	85·16	82·27	78·79	75·25	71·01	70·08	68·22	
0	96·25	$10^3K(a) =$	5·17	4·93	5·14	5·09	5·09	4·99	5·11	5·00	Av. = 5·07 ± 0·07
0	96·25	$10^3K(b) =$	5·17	4·93	5·11	5·09	5·09	4·99	5·06	4·97	Av. = 5·05 ± 0·07
4·0	96·25	$10^3K(c) =$	4·89	4·70	4·88	4·84	4·82	4·73	4·81	4·73	Av. = 4·80 ± 0·06
3·5	96·40	$10^3K(d) =$	5·20	4·97	5·16	5·10	5·05	4·90	4·96	4·85	Av. = 5·02 ± 0·10

NaCl; aq. acetone, 80% by vol. = 75·9% by wt.; $\varepsilon = 32{\cdot}0$; $\eta = 0{\cdot}00700$.

		$10^4c =$	2·636	5·331	6·003	8·564	12·119	13·481	16·356	18·385	
a (Å)	Λ_0	$\Lambda =$	75·00	73·31	72·92	71·66	70·21	69·81	68·72	68·25	
0	78·60	$10^3K(a) =$	3·3	3·4	3·3	3·3	3·2	3·5	3·2	3·5	Av. = 3·3 ± 0·1
0	78·60	$10^3K(b) =$	3·3	3·4	3·3	3·3	3·3	3·4	3·3	3·4	Av. = 3·3 ± 0·05
4·0	78·60	$10^3K(c) =$	2·7	2·8	2·7	2·7	2·7	2·8	2·7	2·8	Av. = 2·7 ± 0·05
4·0	78·70	$10^3K(d) =$	2·7	2·8	2·7	2·65	2·6	2·7	2·5	2·65	Av. = 2·7 ± 0·06

HCl; aq. acetone, 80%.

		$10^4c =$	4·624	5·558	6·386	7·704	9·116	
a (Å)	Λ_0	$\Lambda =$	103·2	102·6	102·2	101·5	100·9	
0	108·50	$10^3K(a) =$	5·8	5·5	6·0	5·8	6·1	Av. = 5·5 ± 0·35
0	108·50	$10^3K(b) =$	5·6	5·3	5·7	5·7	6·0	Av. = 5·6 ± 0·2
4·0	108·50	$10^3K(c) =$	4·4	4·3	4·7	4·5	4·5	Av. = 4·5 ± 0·1
4·0	108·55	$10^3K(d) =$	5·6	5·3	5·6	5·3	5·4	Av. = 5·4 ± 0·1

$HClO_4$; aq. acetone, 90%.

		$10^4c =$	2·304	3·452	4·503	5·676	6·319	8·735	10·612	11·929
a (Å)	Λ_0	$\Lambda =$	131·95	130·75	130·0	129·05	128·7	127·3	126·2	125·65
4·0	137·70	calc. (*c*) =	132·1	130·9	130·0	129·1	128·7	127·2	126·2	125·65
5·0	137·80	calc. (*d*) =	132·0	130·7	129·8	128·9	128·5	127·2	126·3	125·8

$NaClO_4$; aq. acetone, 90%.

		$10^4c =$	1·579	1·821	3·205	4·696	5·157	6·151	7·782	9·423
a (Å)	Λ_0	$\Lambda =$	127·5	127·7	126·0	124·7	124·1	123·6	122·5	121·5
4·0	132·20	calc. (*c*) =	127·6	127·3	125·8	124·5	124·2	123·4	121·8	121·5
4·5	132·60	calc. (*d*) =	127·8	127·4	125·8	124·5	124·2	124·0	122·5	121·6

$HClO_4$; aq. acetone, 80%.

		$10^4c =$	5·522	5·727	7·760	7·853	10·040	10·989
a (Å)	Λ_0	$\Lambda =$	124·8	124·8	124·0	124·2	123·7	123·3
6·0	130·10	calc. (*c*) =	125·0	124·9	124·1	124·1	123·3	123·0
5·0	130·20	calc. (*d*) =	125·0	124·9	124·2	124·1	123·5	123·3

$NaClO_4$; aq. acetone, 80%.

		$10^4c =$	4·088	5·154	6·609	8·465	9·029	11·949	12·213	15·353
a (Å)	Λ_0	$\Lambda =$	95·24	94·61	94·23	93·53	93·47	92·65	92·62	91·92
5·0	99·25	calc. (*c*) =	95·25	94·79	94·24	93·62	93·45	92·65	92·58	91·84
4·5	99·35	calc. (*d*) =	95·23	94·74	94·18	93·59	93·42	92·68	92·62	91·97

TABLE 2. *Dissociation constant of* $HClO_4$ *in* 90% *acetone from spectrophotometry at* 525 mμ *and* 25° (K_{HCl} taken as 0·00305).

10^3[HCl] ...	2·36	2·83	3·37	4·10	4·77	5·48	6·20	6·83	7·52	8·29
10^3[$HClO_4$]	1·78	2·25	2·72	3·24	3·71	4·16	4·61	5·06	5·51	5·85
10^3K	5·5	4·8	4·6	4·7	4·8	4·95	5·1	5·1	5·15	5·5

Average = 5·0 ± 0·25

Experimental

The conductance bridge, cell, and associated apparatus have been described elsewhere [7] together with the method of cell calibration. " AnalaR " sodium chloride was heated to constant weight at 500—600° in a platinum dish before stock solutions were prepared by weight. To make sodium perchlorate solutions, " AnalaR " sodium carbonate was dried at 260—270°, a quantity weighed into a tared flask, 50% " AnalaR " perchloric acid of known concentration added through a reflux condenser to trap spray, the solution brought to the boil, and the flask reweighed after being washed down. To check the concentration, a quantity was reconverted by a H^+ ion resin column and titrated. Ordinary-grade lithium chloride was recrystallised from conductance water, and the crystals were dried at 120—130° before a stock solution was prepared by weight. A check by gravimetric chloride analysis showed the crystals to be >99·95% anhydrous. Stock solutions of " AnalaR " hydrochloric acid in conductance water were analysed by gravimetric chloride analysis.

AnalaR acetone was dried by storage over calcium chloride for at least 24 hr., filtered quickly into a distillation apparatus, and the middle fraction of distillate collected. The density of this (100 ml. sample, 25°) was 0·7848 in every case, and interpolation on the data of Dippy and Hughes [8] showed the water content to be 0·46% by wt. (0·36% by vol.); due allowance was made for this. By 80% and 90% acetone is meant 4 : 1 and 9 : 1 acetone : water by vol. The specific conductances of these solvents were in the range 3—10 gemmho. The viscosities (η) and dielectric constants (ε) were obtained by interpolation from published data.[9,10] Each set of results in Table 1 represents two " runs."

A Hilger " Uvispek " spectrophotometer was used, and for this work a stock solution of *m*-Cresol Purple was made by shaking an excess of it with 80% or 90% acetone and filtering.

One of us (V. M. A.) is indebted to the D.S.I.R. for a research grant.

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University College of Wales, Aberystwyth. [*Received, August 31st,* 1960.]

[7] Davies, *J.*, 1937, **432**; Davies and Monk, *J.*, 1949, **413**.
[8] Dippy and Hughes, *J.*, 1954, 958.
[9] " International Critical Tables," McGraw-Hill Book Co., New York, 1930; Olson and Konecny, *J. Amer. Chem. Soc.*, 1953, **75**, 5801.
[10] Akerlöf, *J. Amer. Chem. Soc.*, 1932, **54**, 4125.

NOTES.

352. *The Adsorption of Uranyl Sulphate from 20% Methanol by an Anion-exchange Resin.*

By D. E. B. Morgans and C. B. Monk.

Several attempts have been made [1,2] to establish the formulæ of the uranyl sulphate complexes which are adsorbed from solution by anion-exchange resins. Among the suggestions arising from these are [2] (*a*) the complex on the resin is $UO_2(SO_4)_n^{(2-2n)}$ where $n \geqslant 2$, (*b*) $n = 3$ or alternatively an equal mixture of $n = 2$ and sulphate ions. However, there is little evidence from other sources to suggest that $UO_2(SO_4)_3^{4-}$ can be formed. Ahrland [3] roughly estimated the complexity constant of this species in aqueous solution but could not substantiate it by spectrophotometric measurements. This is in accord with similar work [4] and with conclusions derived from solvent extractions.[5] For the present work, 20% methanol has been used, since this is somewhat better than water for promoting complex formation.

[1] Lower, U.S. Atomic Energy Comm., AECD–4113. O'Connor, *ibid.*, ACCO 61, 1954.
[2] Arden and Wood, *J.*, 1956, 1596; Arden and Rowley, *ibid.*, 1957, 1709.
[3] Ahrland, *Acta Chem. Scand.*, 1951, **11**, 1151.
[4] Davies and Monk, *Trans. Faraday Soc.*, 1957, **53**, 442.
[5] McDowell and Baes, *J. Phys. Chem.*, 1958, **62**, 77; Allen, *J. Amer. Chem. Soc.*, 1958, **80**, 4133.

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Experimental.—Deacidite FF was equilibrated with sodium chloride solution, washed, and semi-dried on a Buchner funnel. Before use, the resin was dried (P_2O_5) for 48 hr. at room temperature (40 hr. was a safe minimum); this is superior to drying at 110° since Lower [1] found that heating converts part of a sulphated resin into a non-convertible form, and furthermore, Deacidite becomes brittle above 50°. About 0·5 g. samples were weighed into centrifuge tubes fitted with high-porosity bases.[3] To determine the resin capacity, 0·5N-potassium nitrate was passed through; it was 3·86 ± 0·005 mequiv. of Cl^-/g. of dry resin.

For the exchange work, 0·00569M-uranyl sulphate containing sulphuric acid was dripped through till spectrophotometric estimates of the uranyl concentration (at 300 mμ) were constant. This took 150—200 ml. and 40 hr. The resin in its tube was centrifuged for 1 hr. at [6] 2500 rev./min., then eluted with 0·5M-sodium chloride at 5 drops/min.; this took 150 ml. (ferrocyanide test). Uranium in the eluate was estimated by weighing the oxinate, and sulphate was weighed as barium salt.

The pH of the influent was found by Thymol Blue, the colour being matched against 20% methanol solutions of perchloric acid by spectrophotometer at 540 mμ. The HSO_4^- content of the eluate was found likewise with Methyl Orange and standard sulphuric acid at 540 mμ, the elution process being assumed to be $RHSO_4 + Cl^- \rightleftharpoons RCl + HSO_4^-$. Although the eluate contained uranium, this should not influence the HSO_4^- estimate since it was present mainly as UO_2SO_4.

Adsorption of uranyl, sulphate, and bisulphate ions by Deacidite FF (mmoles/g. of resin).

$-\log [H^+]$, influent	1·90	1·66	1·53	1·42	1·30	1·16	1·13	1·05	0·95	0·85	0·75	0·66	0·51
Total $SO_4^{2-} = b$	3·20	3·39	3·36	3·31	3·31	3·36	3·45	3·39	3·56	3·57	3·69	3·75	3·88
$HSO_4^- = d$	0·18	0·22	0·33	0·39	0·35	0·56	0·63	0·71	0·89	1·10	1·35	1·69	2·10
Total $UO_2^{2+} = x$	1·27	1·35	1·24	1·22	1·20	1·08	1·06	1·03	0·95	0·88	0·81	0·69	0·53
Free SO_4^{2-} ($n = 2$)	0·48	0·47	0·55	0·48	0·56	0·64	0·70	0·62	0·77	0·71	0·72	0·68	0·72
Capacity (calc., *a*)	3·68	3·86	3·91	3·79	3·87	4·00	4·15	4·01	4·33	4·28	4·41	4·43	4·60
HSO_4^- (calc.)	0·25	0·09	0·31	0·35	0·39	0·63	0·67	0·73	0·89	1·03	1·17	1·41	1·73
Capacity (calc., *b*)	3·75	3·73	3·89	3·75	3·91	4·07	4·19	4·03	4·33	4·21	4·23	4·15	4·23

Results and Discussion.—The analytical results and relevant calculations are shown in the Table. With x, b, and d as defined in the Table, then nx = complexed sulphate, $b - nx - d$ = free sulphate. Thus the negative charge on the resin = $(2n - 2)x + d + 2(b - nx - d) = 2b - d - 2x$, so than n cannot be deduced from the analysis. A further feature is that, from the Cl^- capacity, $2b - d - 2x$ should be 3·86 mequiv./g., and as the sixth row shows, there is satisfactory accord above pH = 1, but below this the capacity apparently increases. A possible explanation is that the SO_4^{2-} and HSO_4^- determinations include entrapped or permeated free acid, and there is evidence to support this view for, except for the three most acidic solutions, the sum $2x + d$(exptl.) = 2·79 ± 0·05. This produces the HSO_4^- (calc.) values of the seventh row and the last row of capacity values. The latter are still a little high at low pH's but they have not been corrected for the SO_4^{2-} of the free acid (the Kraus and Moore correction [7] proved negligible).

The conclusions that can be drawn are that the resin species are $R_2UO_2(SO_4)_n^{(2n-n)}$ ($n = 1$ and/or 2), R_2SO_4, and $RHSO_4$. If $n = 1$ only, the amounts of R_2SO_4 are greater than those shown in the fourth row by x. Since the quantity of adsorbed uranium falls off at lower pH's, where the solution contains higher concentrations of free UO_2^{2+} (there is less SO_4^{2-} to associate with it and HSO_4^- does not appear to do so), $n = 1$ only seems unlikely. There is the possibility that the resin species is a mixture with $n = 1$ and 2 and there is no R_2SO_4, but this takes no account of the equilibrium $R_2UO_2(SO_4)_2 \rightleftharpoons R_2SO_4 + UO_2SO_4$ (soln.).

One of us (D. E. B. M.) is indebted to the University College of Wales for the award of a Sir Garrod Thomas fellowship.

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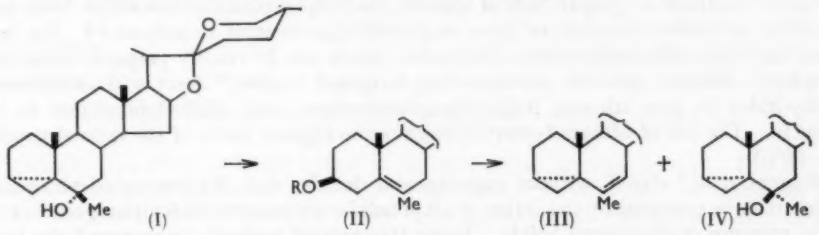
[6] Arden, private communication.
[7] Kraus and Moore, *J. Amer. Chem. Soc.*, 1953, **75**, 1457.

XUM

353 3α,5-*Cyclo*-6β-*methyl*-25D-*spirostan*-6α-*ol and* 3α,5-*Cyclo*-6α-*methyl*-25D-*spirostan*-6β-*ol.*

By G. H. R. Summers.

Recently it has been shown [1] that reaction of methylmagnesium iodide with 3α,5-cyclo-6-oxo-steroids yields the 6α-tertiary alcohols. Thus the compound, m. p. 183—185°, $[\alpha]_D$ −52°, prepared from 3α,5-cyclo-25D-spirostan-6-one by Burn *et al.*[2] is therefore 3α,5-cyclo-6β-methyl-25D-spirostan-6α-ol (I). These workers also isolated in small quantity a second substance, m. p. 175°, $[\alpha]_D$ −130°, believed to be the epimeric tertiary alcohol. Although its analysis and chromatographic properties agree with this formulation, its high negative rotation points to a structure other than that of a cyclosteroid. We now describe the synthesis of authentic 3α,5-cyclo-α-methyl-25D-spirostan-6β-ol.



The alcohol (I) prepared by the method of Burn *et al.*[2] rearranged in presence of toluene-*p*-sulphonic acid in dioxan to 6-methyl-25D-spirost-5-en-3β-ol (II; R = H) the toluene-*p*-sulphonate of which was converted by potassium acetate in boiling aqueous acetone into 3α,5-cyclo-6-methyl-25D-spirost-6-ene (III) and 3α,5-cyclo-6α-methyl-25D-spirostan-6β-ol (IV), m. p. 173°, $[\alpha]_D$ −39°. Both these compounds were rearranged to 6-methyl-25D-spirost-5-en-3β-yl acetate (II; R = Ac) by sulphuric acid in acetic acid. The product of Burn *et al.*[2] is probably 6-methyl-25D-spirost-5-en-3β-ol (II; R = H), formed by rearrangement during the isolation of the alcohol (I). Alcohol (II; R = H) was prepared and had m. p. and $[\alpha]_D$ close to those of the product of Burn *et al.*[2]

Experimental.—$[\alpha]_D$ were measured for $CHCl_3$ solutions.

6-*Methyl*-25D-*spirost*-5-*en*-3β-*yl toluene*-p-*sulphonate.* 6-Methyl-25D-spirost-5-en-3β-ol (5·7 g.) in pyridine (40 ml.) was left at room temperature overnight with toluene-*p*-sulphonyl chloride (6 g.), ice-cold dilute sulphuric acid was added, the product was extracted with chloroform, and the extract washed successively with water, sodium hydrogen carbonate solution, and water. Evaporation of the dried extract gave 6-*methyl*-25D-*spirost*-5-*en*-3β-*yl toluene*-p-*sulphonate*, m. p. 165—166° (decomp.) (from ethyl acetate), $[\alpha]_D$ −100° (*c* 1·1) (Found: C, 72·1; H, 8·5. $C_{35}H_{50}O_5S$ requires C, 72·1; H, 8·65%). Unlike the ester of 6-methylcholesterol [1] this did not decompose on storage.

3α,5-*Cyclo*-6-*methyl*-25D-*spirost*-6-*ene and* 3α,5-*cyclo*-6α-*methyl*-25D-*spirostan*-6β-*ol.* The preceding ester (3·5 g.) was refluxed with potassium acetate (3·5 g.) in acetone (150 ml.) and water (45 ml.) for 3 hr. The acetone was removed under reduced pressure and the product extracted with ether, washed with water, dried (Na_2SO_4), and recovered as an oil which was chromatographed on aluminium oxide (90 g.). Elution with pentane–benzene (9 : 1; 6 × 200 ml.) gave an oil (165 mg.) which on crystallisation from acetone gave 3α,5-*cyclo*-6-*methyl*-25D-*spirost*-6-*ene* as plates, m. p. 106—110°, $[\alpha]_D$ −144° (*c* 1·1) (Found: C, 81·4; H, 10·3. $C_{28}H_{42}O_2$ requires C, 81·9; H, 10·3%). Elution with benzene (26 × 200 ml.) and benzene–ether (9 : 1; 8 × 200 ml.) gave 3α,5-*cyclo*-6α-*methyl*-25D-*spirostan*-6β-*ol* (2·12 g.), m. p. 170—173° (from acetone), $[\alpha]_D$ −39° (*c* 1·2) (Found: C, 78·4; H, 10·4. $C_{28}H_{44}O_3$ requires C, 78·5; H, 10·4%). This compound had m. p. 144—165° on admixture with the isomeric 6α-alcohol.

[1] Davis, Julia, and Summers, *Bull. Soc. chim. France*, 1960, 742.
[2] Burn, Ellis, Petrow, Stuart-Webb, and Williamson, *J.*, 1957, 4092; see also Grenville, Patel, Petrow, Stuart-Webb, and Williamson, *J.*, 1957, 4105; Ellis, Petrow, and Waterhouse, *J.*, 1960, 2596.

XUM

Treatment of the hydrocarbon and the 6β-alcohol in acetic acid with a few drops of concentrated sulphuric acid gave after 1 hr. 6-methyl-25D-spirost-5-en-3β-yl acetate, m. p. 216—218°, $[\alpha]_D$ −130° (*c* 1·0) (plates from chloroform–methanol).

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CHEMISTRY DEPARTMENT, UNIVERSITY OF WALES, SWANSEA. [*Received, September 7th,* 1960.]

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354. *Preparation and Infrared Spectra of Trimeric Dialkylphosphinoborines and Some* B-*Halogenated Derivatives.*

By R. H. BIDDULPH, M. P. BROWN, R. C. CASS, R. LONG, and H. B. SILVER.

REPORTED methods of preparation of trimeric dialkylphosphinoborines either have used difficultly accessible materials or have employed high-vacuum techniques.[1-3] We have found that tetra-alkyldiphosphine disulphides, which can be readily prepared from thiophosphoryl chloride and the corresponding Grignard reagent,[4] react with alkali-metal borohydrides to give trimeric dialkylphosphinoborines, with dialkylphosphines as by-products. The use of lithium borohydride gave the highest yields of the desired product (50—60%).

Wagner *et al.*[2] stated, without experimental details, that *B*-halogenated phosphinoborines may be prepared by the action of alkyl halides on trimeric dialkylphosphinoborines in the presence of aluminium halide. Using this general method, we prepared the hexachloro-derivative of trimeric dimethylphosphinoborine and the hexa-chloro-, -bromo-, and -iodo-derivatives of trimeric diethylphosphinoborine. The chloro-derivatives were obtained in good yields by refluxing the phosphinoborine in butyl chloride in the presence of aluminium chloride. Similarly, the hexabromide was obtained from the trimer, propyl bromide, and aluminium bromide. However, the iodo-derivative was prepared by adding iodine to a solution of the trimer in ethyl iodide until the colour was no longer discharged. Chemically, the *B*-halogenated phosphinoborines appeared unreactive. Thus trimeric dimethylphosphinodichloroborine was recovered unchanged after being heated with ammonia at 200° for several days or under reflux with diethylamine. It was also unchanged after refluxing with methylmagnesium iodide in ether.

Infrared Spectra (R.H.B.) (see Fig. and Table).—When the boron atom of a simple molecule BX_3 (where X = halogen) is bonded to a donor atom, the B–X stretching frequencies observed are lower than those found in the simple molecule BX_3; *e.g.*, Bellamy *et al.*[5] quote for the B–Cl stretching frequency a range 850—910 cm.$^{-1}$, whereas we have found a range of 690—770 cm.$^{-1}$ for both the phosphinoborines and the co-ordination compounds R_3NBCl_3 where R_3N is triethylamine or pyridine.[6] This lowering of the asymmetric stretching frequency can be explained in view of the changed electronic environment of the boron atoms owing to the donation of electrons to the bond system by the phosphorus or nitrogen atoms. When X is hydrogen the B–H stretching frequencies which we found occurred at the lower end of the range 2350—2630 cm.$^{-1}$ quoted by Bellamy *et al.*[5] for boron hydrides. The B–H deformation frequencies observed for these phosphinoborines correspond closely to those found previously in the hydrides and are similar to

[1] Burg and Wagner, *J. Amer. Chem. Soc.*, 1953, **75**, 3872.
[2] Wagner, Caserio, Evleth, Freeman, and Stewart, Abs. Papers, 135th Meeting Amer. Chem. Soc., April 1959, p. 49–o.
[3] Burg and Slota, *J. Amer. Chem. Soc.*, 1960, **82**, 2145.
[4] Kabachnik and Schepeleva, *Izvest Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1949, No. 1, 56; Kosolapoff and Watson, *J. Amer. Chem. Soc.*, 1951, **73**, 5466; Christen, Van Der Linde, and Hooge, *Rec. Trav. chim.*, 1959, **78**, 161; Kuchen and Buckwald, *Angew. Chem.*, 1959, **71**, 162; Issleib and Tzschach, *Chem. Ber.*, 1959, **92**, 704.
[5] Bellamy, Gerrard, Lappert, and Williams, *J.*, 1958, 2412.
[6] Katritzky, *J.*, 1959, 2049; Greenwood and Wade, *J.*, 1960, 1130; Waddington and Klanberg, *J.*, 1960, 2339.

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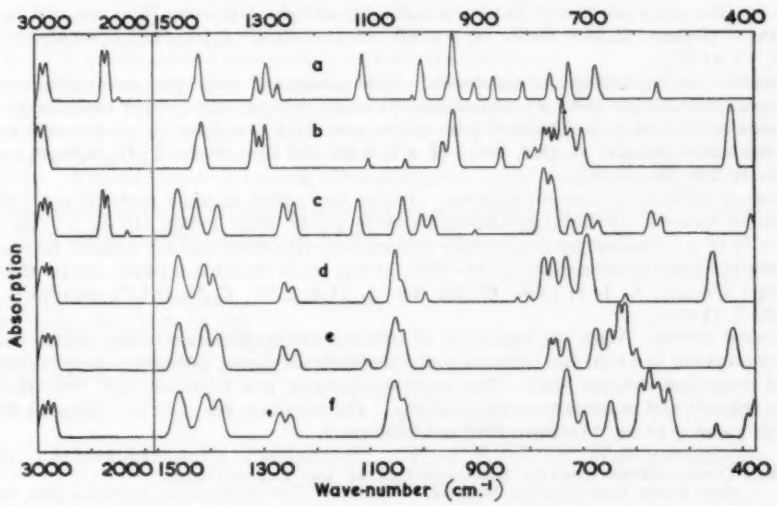
Assignments of bands observed in the spectra of $[R_2P{\cdot}BX_2]_3$.

R	Me		Me		Et		Et		Et		Et		
X	H		Cl		H		Cl		Br		I		Ref.
CH stretch	2910		2918		2870	2922	2859	2911	2852	2905	2855	2910	*a*
	2965		2979		2955		2940		2940		2950		
BH stretch	2332		—		2345	2380	—		—		—		5
	2370												
CH_3 deform. as.	1420		1418		1462		1460		1458		1457		*a*
CH_2 deform. s.	1268	1294	1298	1303	1388		1388		1382		1386		*a*
	1310		1314										
CH_2 scissor	—		—		1422		1412		1410		1410		*a*
CH_2 wag	—		—		1242		1244		1239		1250		*a*
					1260		1260		1258		1268		
BH_2 scissor	1111		—		1118		—		—		—		5
CH_3 rock	938		940		1043		1050		1050		1054		*a*
BH_2 wag	1000		—		982		—		—		—		5
					1003								
B Hal_2 stretch as.	—		738		—		691		620	630	576		
BH_2 rock	557		—		570		—		—		—		
B Hal_2 stretch s.	—		420		—		455		415		<375		

a, Bellamy, " Infra-red Spectra of Complex Molecules," Methuen, London, 1958.

those for the SiH_2 group as found by Ebsworth, Onyszchuk, and Sheppard.[7] This is to be expected, since the stretching force constants calculated from the observed mean BH and SiH are 2·9 and 2·7 $\times$ 10^5 dynes/cm. The bending force constants are probably similar to one another.

Spectra of $(R_2P{\cdot}BX_2)_3$. (*a*) R = Me, X = H; (*b*) R = Me, X = Cl); (*c*) R = Et, X = H; (*d*) R = Et, X = Cl; (*e*) R = Et, X = Br; (*f*) R = Et, X = I.



N.B. The featureless part of the spectra between 1500 and 2000 cm.$^{-1}$ has been omitted.

Experimental.—Trimeric dimethylphosphinoborine. Tetramethyldiphosphine disulphide (9·3 g.) and lithium borohydride (3·3 g.) were ground together and placed in a flask provided with a 5 ft. air-condenser, to the top of which was connected a U-trap cooled in liquid nitrogen. The apparatus was completely flushed with dry nitrogen. The flask was heated to 250° at atmospheric pressure. After 1 hr. the pressure in the system was reduced to 25 mm. and the heating was continued for a further 3 hr. During the reaction, crystals of the product sublimed

into the air-condenser. The volatile material collected in the U-trap was shown to be dimethylphosphine (0·2 g.) (v. p. at 0° = 342·5 mm.; Wagner and Burg [8] give 342 mm.). The contents of the air-condenser and the reaction flask were extracted with light petroleum (b. p. 40—60°), the solution was chromatographed (Woelm alumina, neutral grade), and the solid (3·5 g.) obtained by evaporation of the eluant was crystallised from methanol, giving trimeric dimethylphosphinoborine, m. p. 87—88° (Burg and Wagner [1] give m. p. 85—86°).

Numerous other preparations which were carried out with sodium and potassium borohydride showed that the amount of dimethylphosphine formed tended to increase (10—30%) whilst the yields of trimeric dimethylphosphinoborine were reduced (20—25%) (yields based on the amount of initial tetramethyldiphosphine disulphide). Use of 2,2′-dimethoxydiethyl ether as a reaction medium in the initial stages offered no advantage.

Trimeric diethylphosphinoborine. A mixture of tetraethyldiphosphine disulphide (12·1 g.) and lithium borohydride (6·5 g.) was heated at 280—300° under nitrogen for 7 hr. Volatile material, assumed to be diethylphosphine (0·3 g.), was collected in a trap cooled at −196°. The mixture was extracted with light petroleum (b. p. 40—60°), and removal of the solvent left an oil (6·15 g.). The crude oil was distilled, giving trimeric diethylphosphinoborine, b. p. 106—108°/0·1 mm., n^{20} 1·5312 (Found: C, 47·0, 46·7; H, 11·9, 12·2. Calc. for $C_{12}H_{36}B_3P_3$: C, 47·1; H, 11·9%). Burg and Slota [3] give b. p. 133—134°/1·5 mm.

Trimeric dimethylphosphinodichloroborine. Trimeric dimethylphosphinoborine (1·22 g.) was heated in butyl chloride (20 c.c.). Aluminium chloride (0·45 g.) was added, and after 5 min. a very vigorous reaction ensued, the mixture became yellow, and hydrogen chloride was evolved. Heating was continued until evolution of hydrogen chloride ceased (1·5 hr.). The mixture was decomposed with water (50 c.c.) and extracted with chloroform. Removal of the solvents gave a residue (2·26 g.) which crystallised from benzene, giving *trimeric dimethylphosphinodichloroborine*, m. p. 393—394° (Found: C, 17·3, 17·5; H, 4·2, 4·4; Cl, 49·6, 50·1. $C_6H_{18}B_3Cl_6P_3$ requires C, 16·8; H, 4·2; Cl, 49·7%).

Trimeric diethylphosphinodichloroborine. In a similar manner this *compound* was prepared from trimeric diethylphosphinoborine (0·22 g.), aluminium chloride (0·13 g.), and butyl chloride (10 c.c.). The crude product (0·35 g.) crystallised from light petroleum (b. p. 40—60°) as rods, m. p. 181·5° (Found: C, 28·9, 28·95; H, 5·9, 6·0; Cl, 41·2, 41·5. $C_{12}H_{30}B_3Cl_6P_3$ requires C, 28·1; H, 5·9; Cl, 41·5%).

Trimeric diethylphosphinodibromoborine. This *compound* was prepared from trimeric diethylphosphinoborine (0·83 g.), aluminium bromide (0·3 g.), and propyl bromide (10 c.c.). The crude solid (1·93 g.) crystallised from chloroform–light petroleum (b. p. 40—60°) as rods, m. p. 304—305° (Found: C, 18·5, 18·7; H, 4·1, 3·85; Br, 61·0, 61·2. $C_{12}H_{30}B_3Br_6P_3$ requires C, 18·5; H, 3·9; Br, 61·5%).

Trimeric diethylphosphinodi-iodoborine. Iodine was added in small portions to a refluxing solution of trimeric diethylphosphinoborine (0·74 g.) in ethyl iodide (10 c.c.). The crude product (2·18 g.) obtained by evaporation was washed with ether and crystallised from carbon tetrachloride–light petroleum (b. p. 40—60°), giving small rhombic crystals, m. p. 325—330° (decomp.) (Found: C, 14·8, 14·6; H, 2·8, 2·6; I, 71·3, 71·7. $C_{12}H_{30}B_3I_6P_3$ requires C, 13·6; H, 2·85; I, 71·6%).

Infrared spectra. With the exception of trimeric diethylphosphinoborine, which is liquid and was prepared as a thin film between potassium bromide plates, substances were examined in pressed potassium chloride discs. The spectrophotometer was a Unicam S.P. 100 fitted with sodium chloride and potassium bromide prisms. The accuracy was ±5 cm.$^{-1}$ between 375 and 2000 cm.$^{-1}$ and ±10 cm.$^{-1}$ between 2000 and 3500 cm.$^{-1}$.

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COX LANE, CHESSINGTON, SURREY. [*Received, September 26th*, 1960.]

[7] Ebsworth, Onyszchuk, and Sheppard, *J.*, 1958, 1453.
[8] Wagner and Burg, *J. Amer. Chem. Soc.*, 1953, **75**, 3869.

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355. *The Diazo-exchange Reaction studied with Nitrogen-15: p-Nitrophenyldiazonium Chloride Solution.*

By P. F. Holt and C. J. McNae.

A previous paper [1] described the application of nitrogen-15 to the study of the diazo-exchange in which a diazonium group appears to change places with an amino-group. Of the two mechanisms which had been suggested one was rejected. This, due to Bamberger,[2] assumed an equilibrium between diazonium salts and nitrous acid and suggested that the acid diazotised free amino-groups. No such equilibrium could be observed; when potassium [^{15}N]nitrite was added to diazonium salts it was not incorporated in the diazonium ion.

In support of Bamberger's theory, Bucherer and Wolff [3] claimed to have demonstrated that nitrous acid was present in a solution of *p*-nitrophenyldiazonium chloride purified by converting it into sodium *p*-nitrophenylisodiazoate and acidifying this. This observation appeared directly contradictory to our results. We therefore repeated the experiments of the previous paper on a solution of *p*-nitrophenyldiazonium chloride.

Experimental.—*p*-Nitroaniline (B.D.H.), recrystallised to m. p. 145·5—146·5° (lit., 146°) (0·340 g.) was dissolved in hydrochloric acid (8 ml.; 2N) and water (17 ml.), and the solution was diazotised with sodium nitrite (0·215 g.). A solution containing potassium [^{15}N]nitrite (0·0589 g.; 35·8 atom % of nitrogen-15) was then added, and the mixture left for 4 days at 0—3°. Free nitrous acid was then removed by addition of urea, and the mixture poured into 2-naphthol (0·410 g.) in aqueous sodium carbonate (1 g. in 100 ml.). The precipitated 1-*p*-nitrophenylazo-2-naphthol was washed with water (150 ml.), recrystallised once from dimethylformamide, and thoroughly dried; it had m. p. 251° (lit.,[4] 251—252°).

The nitrogen-15 abundance in the nitrogen of the azo-compound was 0·40 atom % (atmospheric abundance, 0·37 atom %). If the equilibrium existed, some nitrogen-15 would have been incorporated into the diazonium ion, resulting in a calculated abundance for the product of 6·93 atom % of nitrogen-15 under the experimental conditions.

This result confirms the view that a mechanism involving an equilibrium between nitrite and diazonium ions is unacceptable and leaves the mechanism suggested by Bayer,[5] involving the formation and decomposition of a triazen, as the only reasonable mechanism suggested so far. It is possible that Bucherer and Wolff failed to free their sodium *p*-nitrophenylisodiazoate from nitrite. Any mechanism involving the nuclear nitro-group has already been eliminated.[1]

We are grateful to Dr. D. H. Tomlin who assayed the nitrogen samples, and to the Department of Scientific and Industrial Research for a grant (to C. J. M.).

The University, Reading. [*Received, October 17th*, 1960.]

[1] Holt, Hopson-Hill, and McNae, *J.*, 1960, 2245.
[2] Bamberger, *Ber.*, 1895, **28**, 827.
[3] Bucherer and Wolff, *Ber.*, 1909, **42**, 881.
[4] Bamberger and Meimberg, *Ber.*, 1895, **28**, 1894.
[5] Bayer, D.R.-P. 1890, 51,576.

356. *Phosphonitrilic Derivatives. Part VI.*[1] *N-Methyltrichlorophosphinimine Dimer.*

By A. C. Chapman, W. S. Holmes, N. L. Paddock, and H. T. Searle.

Products of the condensation of phosphorus pentachloride with amides have often been described; a large number of such derivatives, apparently containing the P=N group, have been obtained by Kirsanov and his co-workers.[2] The parent compound, trichlorophosphophinimine $NH{:}PCl_3$, is believed to be formed in the reaction between phosphorus

[1] Part V, Chapman, Paine, Searle, Smith, and White, *J.*, 1961, 1768.
[2] Kirsanov, *Khim. i Prim. Fos. Akad. Nauk S.S.S.R. Trudy I-O Konferents*, 1955, 99 (Pub. 1957).

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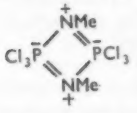
pentachloride and ammonium chloride,[3] subsequently condensing either with itself or with further phosphorus pentachloride to give the linear phosphonitrilic derivatives previously described.[4] Gilpin [5] prepared *N*-phenyltrichlorophosphinimine by reaction of aniline hydrochloride with phosphorus pentachloride; we report here the preparation of dimeric *N*-methyltrichlorophosphinimine, which displays some new structural features.

The compound has the dimeric formula $(CH_3{\cdot}N{:}PCl_3)_2$; it is a non-conductor in nitrobenzene. Its molecular weight is independent of temperature (5—74°) and of the dielectric constant of the solvent (2·3—34·8). The two monomer units are therefore united by primary valencies rather than by dipolar forces. The spectroscopic data agree most nearly with a centrosymmetric structure in which the phosphorus and nitrogen atoms form a 4-membered planar ring. The ring bonds are strong, as Mortimer [6] found a minimum average value for E[P–N] of 74·3 kcal. mole^{-1}. The infrared peak at 2812 cm.$^{-1}$ is characteristic of an *N*-methyl group bearing an unshared pair of electrons,[7] but its low intensity compared with that of the C–H stretching band at 2941 cm.$^{-1}$ suggests some delocalisation. The transfer of one electron from each nitrogen atom would allow the formation of polar $d\pi$–$p\pi$ bonds, one of a pair of symmetrically related structures being as shown (inset), the ring bonds now resembling those in the phosphonitrilic chlorides, in which [8] E[P–N] = 72·3 kcal. mole^{-1}. This interpretation is consistent with the absence of a peak in the region 1290—1325 cm.$^{-1}$ associated [9] with the P·N·CH_3 group; the strong peak at 847 cm.$^{-1}$ may correspond to a P–N stretching vibration, normally expected [9,10] in the range 680—750 cm.$^{-1}$. If the bonds are of the type proposed, the natural ring angle at the nitrogen atoms would be close to 120°, and at the phosphorus atoms should not be less than 90°. It is remarkable that a dimer is formed, rather than a trimer in which the angular requirements could be easily satisfied by slight puckering of the ring. Related compounds, notably the phosphoric imido-amides RN:P(O)·NHR, are often associated,[11] and Michaelis [12] has postulated 4-membered ring structures for several classes of phosphorus–nitrogen compound on the basis of their molecular weights. The type of structure deduced here for *N*-methyltrichlorophosphinimine may therefore occur frequently.



Experimental.—Methylammonium chloride (74·3 g., 1·1 moles), phosphorus pentachloride (208·5 g., 1 mole), and *sym*-tetrachloroethane (1 l.), all commercial materials, were heated together under reflux for 5 hr.; when reaction had practically ceased, the amount of hydrogen chloride evolved corresponded closely to that required by the reaction $Me{\cdot}NH_3Cl + PCl_5 \longrightarrow MeN{:}PCl_3 + 3HCl$. The excess of salt was filtered off, and the solvent distilled off *in vacuo* (yield 150 g., 90%). The product was recrystallised from carbon tetrachloride and sublimed at 150°/0·5 mm., giving hygroscopic monoclinic needles of dimeric *N-methyltrichlorophosphinimine*, m. p. 160° (decomp.) (Found: C, 7·1; H, 1·8; N, 8·5; Cl, 63·4; P, 18·9. CH_3Cl_3NP requires C, 7·2; H, 1·8; N, 8·4; Cl, 64·0; P, 18·6%). Phosphorus was estimated as magnesium pyrophosphate or as phosphomolybdate after hydrolysis by a solution of silver nitrate in nitric acid.

Molecular weights were determined in carbon tetrachloride with a special Menzies–Wright ebulliometer, in which the solvent was dried *in situ* by circulation through activated alumina before the sample was added to it by breakage of a phial within the apparatus. They were also determined cryoscopically in benzene and in nitrobenzene; the values obtained by the three methods (315, 348, 330) are close to that (333) for the dimer. The molar conductance

[3] Proctor, Thesis, London, 1958.
[4] Lund, Paddock, Proctor, and Searle, *J.*, 1960, 2542; Becke-Goehring and Koch, *Chem. Ber.*, 1959, **92**, 1188.
[5] Gilpin, *Amer. Chem. J.*, 1897, **19**, 352.
[6] Mortimer, *Chem. and Ind.*, 1960, 444.
[7] Braunholtz, Ebsworth, Mann, and Sheppard, *J.*, 1958, 2780.
[8] Hartley, Paddock, and Searle, *J.*, 1961, 430.
[9] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 2nd edn., p. 323.
[10] Holmstedt and Larsson, *Acta Chem. Scand.*, 1951, **5**, 1179.
[11] Kosolapoff, " Organo-Phosphorus Compounds," Wiley, New York, 1950, p. 295.
[12] Michaelis, *Annalen*, 1903, **326**, 129.

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of the compound in nitrobenzene at 25° was near 1·7 ohm^{-1} mole^{-1} cm.^{2} over the range (0·5—2·0) × 10^3 l. mole^{-1}. Since values near 30 ohm^{-1} mole^{-1} cm.^{2} are obtained [13] for 1 : 1 electrolytes in nitrobenzene, the small conductance observed is attributed to ionic impurities (principally water or hydrogen chloride), and *N*-methyltrichlorophosphinimine itself is taken to be a non-electrolyte.

Infrared spectra, for CS_2 or CCl_4 solutions, were obtained with a Perkin–Elmer model 21 spectrometer, calibrated with polystyrene. Raman spectra, for CS_2 or benzene solutions, were obtained with a Hilger direct-recording Raman spectrograph. Depolarisation factors were determined approximately by Edsall and Wilson's method.[14] Solutions were prepared and cells were filled inside a dry-box. The following fundamental frequencies were observed, relative intensities and state of polarisation, where appropriate, being also given.

Raman lines (cm.$^{-1}$): 204ms,dp, 268s,dp, 352vs,p, 412w,dp, 458m,dp, 544s,dp, 2946m, 2999vw.

Infrared bands (cm.$^{-1}$): 434m, 575s, 658s, 700m, 747vw, 847vs, 1162s, 1184s, 1210s, 1429m, 1461m, 2812w, 2941m, 2996m.

Since the two methyl groups in a dimeric molecule will be very weakly coupled, the Raman active–infrared active methyl vibrations are likely to be unresolved, leading to apparent Raman–infrared coincidences for methyl group vibrations irrespective of molecular symmetry. All the bands above 1150 cm.$^{-1}$ are tentatively assigned to methyl group vibrations, and the two remaining series of bands are mutually exclusive, leading to the conclusion that the molecule is centrosymmetrical, the phosphorus and nitrogen atoms alternating in a 4-membered ring. These remaining bands are fewer than predicted on the basis of the proposed symmetry [15 Raman lines, either all polarised (C_i) or 10 polarised (C_{2h}), and 15 infrared bands], but this is not unexpected, because many of the predicted infrared bands are probably of too low a frequency to be observed, while some of the weaker Raman lines may have escaped observation.

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[13] Kraus and Witschonke, *J. Amer. Chem. Soc.*, 1947, **69**, 2472.
[14] Edsall and Wilson, *J. Chem. Phys.*, 1938, **6**, 124.

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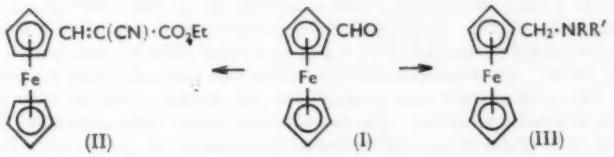
357. *Some Substituted Ferrocenes.*

By I. K. Barben.

Formylferrocene [1] (I) condensed with ethyl cyanoacetate at room temperature, in ethanol containing a trace of piperidine, to give ethyl α-cyano-β-ferrocenylacrylate (II). Condensation also took place in boiling benzene containing a little piperidine and acetic acid.[2] No addition of phenylmagnesium bromide to this acrylate occurred even in the



presence of cuprous chloride.[3] 2-Dimethylaminoethylamine reacted with the ferrocene aldehyde (I) and the product was reduced by sodium borohydride to (2-dimethylaminoethylaminomethyl)ferrocene (III; R = CH_2·CH_2·NMe_2, R′ = H) which was isolated as a

[1] Graham, Lindsey, Parshall, Peterson, and Whitman, *J. Amer. Chem. Soc.*, 1957, **79**, 3416.
[2] Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Amer. Chem. Soc.*, 1941, **63**, 3452.
[3] Brandström and Forsblad, *Arkiv Kemi*, 1954, **6**, 561.

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dihydrochloride. This same aldehyde and aniline in boiling toluene containing a trace of phosphoryl chloride [4] gave anilinomethylferrocene (III; R = Ph, R′ = H) after reduction with sodium borohydride. Similarly, 2-pyridylaminomethylferrocene (III; R = 2-C_5H_4N, R′ = H) was obtained, but in better yield when the reactants condensed at 100°. An attempted alkylation of the anilino-derivative (III; R = Ph, R′ = H) with 2-dimethylaminoethyl chloride in boiling xylene in the presence of sodamide failed but chloroacetyl chloride in the presence of triethylamine [5] in ether gave the amide (III; R′ = Ph, R = $CO{\cdot}CH_2Cl$) whence the piperidinoacetyl compound (III; R = $C_5H_{10}N{\cdot}CH_2{\cdot}CO$, R′ = Ph) was obtained.

Experimental.—Ethyl α-cyano-β-ferrocenylacrylate. (*a*) A solution of formylferrocene [1] (1·07 g.) and ethyl cyanoacetate (0·57 g.) in ethanol (10 c.c.) containing a few drops of piperidine deposited red cubes (0·9 g., 58%) of *ethyl α-cyano-β-ferrocenylacrylate*, m. p. 88—90° [from light petroleum (b. p. 60—80°) or ethanol] (Found: C, 62·4; H, 5·1; N, 4·55. $C_{16}H_{15}FeNO_2$ requires C, 62·2; H, 4·9; N, 4·5%).

(*b*) The aldehyde (1·07 g.) and ethyl cyanoacetate (0·57 g.) in benzene (50 c.c.) containing a few drops of piperidine and acetic acid (0·6 g.) were heated under reflux in a Dean and Stark apparatus. When the theoretical amount of water had been collected the benzene solution was washed with water and dried ($MgSO_4$). Evaporation of the solvent left the acrylate ester (1·3 g., 84%).

(2-Dimethylaminoethylaminomethyl)ferrocene. A mixture of formylferrocene (2·14 g.) and 2-dimethylaminoethylamine (0·88 g.) was set aside for several days. The resulting red oil was dissolved in methanol (20 c.c.), and sodium borohydride (0·38 g.) was added, with stirring, during 15 min. After being boiled for a further 15 min. the solution was poured into water and extracted with ether. The dried ($MgSO_4$) solution, on saturation with hydrogen chloride, deposited *(2-dimethylaminoethylaminomethyl)ferrocene dihydrochloride* (1·7 g., 54%), yellow needles (from 1 : 1 ethanol–ether), m. p. 203—205° (decomp.) (Found: C, 50·0; H, 6·4; Fe, 15·3; N, 7·7. $C_{15}H_{23}N_2Fe,2HCl$ requires C, 50·2; H, 6·7; Fe, 15·5; N, 7·8%).

Anilinomethylferrocene. Aniline (1·12 g.) and formylferrocene (2·14 g.) in toluene (50 c.c.) containing phosphoryl chloride (0·1 c.c.) were refluxed in a Dean and Stark apparatus until the theoretical amount of water had been collected. The filtered solution was washed with water and dried ($MgSO_4$). The red oil obtained on evaporation of the solvent was reduced with sodium borohydride as described above. *Anilinomethylferrocene* (2·6 g., 90%), m. p. 85—86°, crystallised as yellow plates from aqueous ethanol (Found: C, 70·1; H, 5·9; N, 5·0. $C_{17}H_{17}FeN$ requires C, 70·1; H, 5·9; N, 4·8%).

2-Pyridylaminomethylferrocene. Similar conditions afforded *2-pyridylaminomethylferrocene* (35%), m. p. 138—140°, as red needles [from light petroleum (b. p. 60—80°)] (Found: C, 66·3; H, 5·4; N, 9·25. $C_{16}H_{16}FeN_2$ requires C, 65·8; H, 5·5; N, 9·6%). When equimolar quantities of the amine and the aldehyde were heated on a steam-bath for 9 hr. and then reduced with sodium borohydride a 62% yield was obtained.

N-Chloroacetylanilinomethylferrocene. Addition of chloroacetyl chloride (0·57 g.) to a stirred ethereal solution of anilinomethylferrocene (1·46 g.) and triethylamine (0·51 g.) gave the *chloroacetyl derivative* (1·49 g., 81%) on removal of the solvent. Recrystallisation from benzene–light petroleum (b. p. 60—80°) afforded yellow needles, m. p. 140—141° (Found: C, 61·6; H, 5·0; Cl, 9·2; Fe, 14·9; N, 3·8. $C_{19}H_{18}ClFeNO$ requires C, 62·1; H, 4·9; Cl, 9·6; Fe, 15·2; N, 3·8%). The chloroacetyl compound (6·7 g.) and piperidine (3·05 g.) were heated under reflux in dry benzene for 10 hr. The filtered benzene solution was extracted with 2N-hydrochloric acid (3 × 20 c.c.). The acid extract was basified and the product isolated with ether as an oil (6 g., 79%) which slowly solidified. Recrystallisation from light petroleum (b. p. 38—42°) gave yellow rods of *N-(piperidinoacetyl)anilinomethylferrocene*, m. p. 71—73° (Found: C, 69·7; H, 7·25; N, 6·75. $C_{24}H_{28}FeN_2O$ requires C, 69·2; H, 6·8; N, 6·7%).

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[4] Weston and Michaels, *J. Amer. Chem. Soc.*, 1951, **73**, 1381.
[5] Suter, Zutter, and Widler, *Annalen*, 1952, **576**, 233.

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